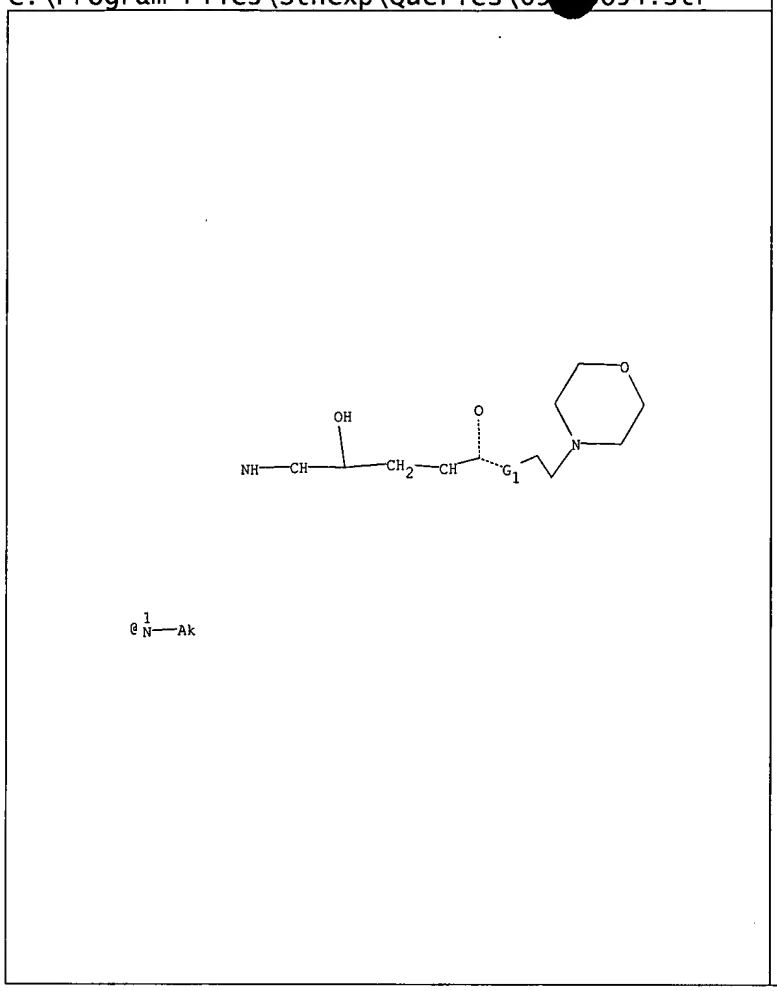
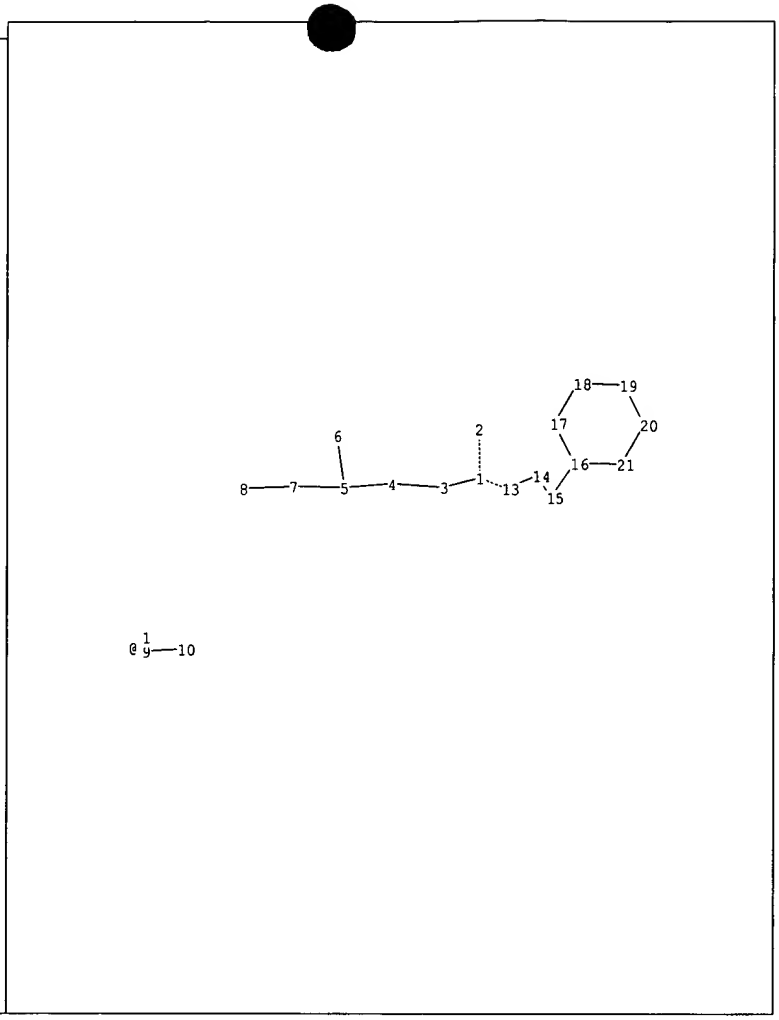
C:\Program Files\Stnexp\Queries\09[redacted]634.str





chain nodes :
1 2 3 4 5 6 7 8 9 10 13 14 15
ring nodes :
16 17 18 19 20 21
chain bonds :
1-2 1-3 1-13 3-4 4-5 5-6 5-7 7-8 9-10 13-14 14-15 15-16
ring bonds :
16-17 16-21 17-18 18-19 19-20 20-21
exact/norm bonds :
1-2 1-13 5-6 7-8 9-10 13-14 15-16 16-17 16-21 17-18 18-19 19-20 20-21
exact bonds :
1-3 3-4 4-5 5-7 14-15

G1:O,NH,[*1]

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
13:CLASS 14:CLASS 15:CLASS 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1611hxl

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

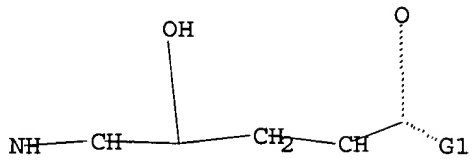
NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	AUG 15	Indexing from 1937 to 1946 added to records in CA/CAPLUS
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003

```
 NEWS 35  AUG 18  Data available for download as a PDF in RDISCLOSURE
 NEWS 36  AUG 18  Simultaneous left and right truncation added to PASCAL
 NEWS 37  AUG 18  FROSTI and KOSMET enhanced with Simultaneous Left and Right
                  Truncation
 NEWS 38  AUG 18  Simultaneous left and right truncation added to ANABSTR

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:10:23 ON 20 AUG 2003

=> fil reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:10:37 ON 20 AUG 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 AUG 2003  HIGHEST RN 569296-21-5
DICTIONARY FILE UPDATES:  18 AUG 2003  HIGHEST RN 569296-21-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09960634.str

L1      STRUCTURE UPLOADED
```

=>
Uploading 09960634.str

L2 STRUCTURE UPLOADED

=> d l2
L2 HAS NO ANSWERS
L2 STR



1
N—Ak

G1 O,NH,[@1]

Structure attributes must be viewed using STN Express query preparation.

=> s l2
SAMPLE SEARCH INITIATED 16:11:39 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 10461 TO ITERATE

9.6% PROCESSED 1000 ITERATIONS 25 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

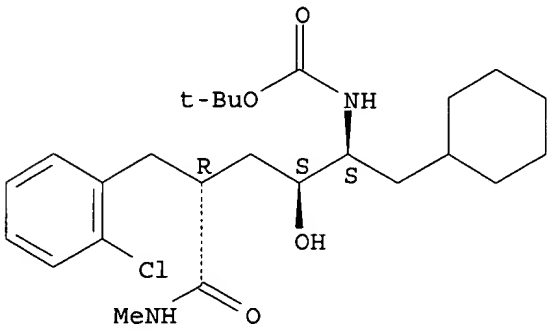
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 203095 TO 215345
PROJECTED ANSWERS: 4260 TO 6200

L3 25 SEA SSS SAM L2

=> d scan

L3 25 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Carbamic acid, [4-[(2-chlorophenyl)methyl]-1-(cyclohexylmethyl)-2-hydroxy-5-(methylamino)-5-oxopentyl]-, 1,1-dimethylethyl ester, [1S-(1R*,2R*,4S*)]- (9CI)
MF C25 H39 Cl N2 O4

Absolute stereochemistry.



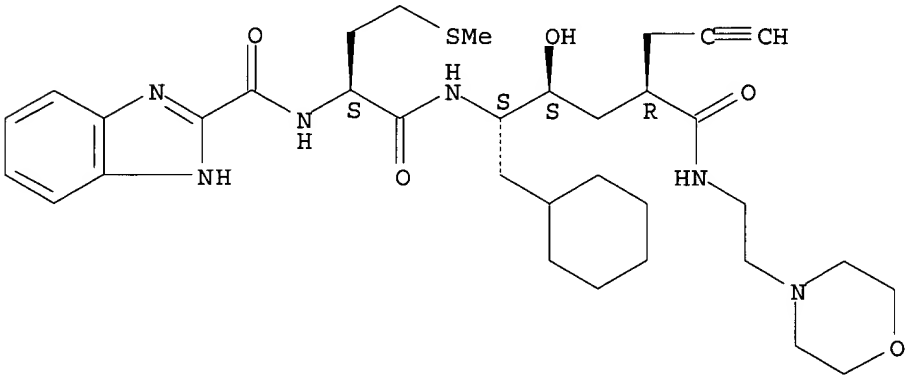
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

```
=>
Uploading 09960634.str

L4      STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4              STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l4
SAMPLE SEARCH INITIATED 16:13:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     39 TO ITERATE

100.0% PROCESSED      39 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          406 TO     1154
PROJECTED ANSWERS:               1 TO       80

L5            1 SEA SSS SAM L4

=> d scan
```

L5 1 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 1H-Benzimidazole-2-carboxamide, N-[(1S)-1-[[[(1S,2S,4R)-1-(cyclohexylmethyl)-2-hydroxy-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]-6-heptynyl]amino]carbonyl]-3-(methylthio)propyl]- (9CI)
MF C34 H50 N6 O5 S

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

```
=> s l4 ful
FULL SEARCH INITIATED 16:14:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    937 TO ITERATE

100.0% PROCESSED     937 ITERATIONS                          107 ANSWERS
SEARCH TIME: 00.00.01

L6          107 SEA SSS FUL L4

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   150.15     150.36

FILE 'CAPLUS' ENTERED AT 16:14:28 ON 20 AUG 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 20 Aug 2003  VOL 139 ISS 8
FILE LAST UPDATED: 19 Aug 2003  (20030819/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l6
L7          22 L6

=> d abs ibib hitstr 1-
YOU HAVE REQUESTED DATA FROM 22 ANSWERS - CONTINUE? Y/(N):
YOU HAVE REQUESTED DATA FROM 22 ANSWERS - CONTINUE? Y/(N):y\
YOU HAVE REQUESTED DATA FROM 22 ANSWERS - CONTINUE? Y/(N):y
```

L7 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB Crystal structures of human memapsin 2 (.beta.-secretase) in complexes with inhibitors OM99-2 and OM99-3 (EVNL*AAEF and ELDL*AVEF, where * is a hydroxyethylene transition state isostere) provide the basis for identifying side chain preferences for inhibitor and substrate interactions. The invention provides compds. that inhibit memapsin 2 activity and selectively inhibit memapsin 2 .beta.-secretase activity relative to memapsin 1 (.beta.-secretase 2) activity. Inhibitors of memapsin 1 were designed and selected from a random sequence combinatorial inhibitor library based on OM99-2. Carrier peptide-inhibitor conjugates employ a peptide derived from a segment of the HIV tat tat protein (residues 47-57) and an oligo(D-arginine) moiety. The compds. are employed in methods to inhibit memapsin 2 .beta.-secretase activity, in the treatment of Alzheimer's disease, in the inhibition of hydrolysis of a .beta.-secretase site of a .beta.-amyloid precursor protein, and to decrease .beta.-amyloid protein in in vitro samples and in mammals. Proteins of memapsin 2 assocd. with compds. of the invention are crystd. and their at. coordinates detd. by x-ray crystallog.

ACCESSION NUMBER: 2003:376558 CAPLUS
DOCUMENT NUMBER: 138:396233
TITLE: Design of .beta.-secretase inhibitors for treatment of Alzheimer's disease based on crystal structures of .beta.-secretase and side chain interactions in inhibitor complexes
INVENTOR(S): Ghosh, Arun K.; Tang, Jordan; Bilcer, Geoffrey; Chang, Wanpin; Hong, Lin; Koelsch, Gerald; Loy, Jeff; Turner, Robert T., III
PATENT ASSIGNEE(S): Oklahoma Medical Research Foundation, USA; University of Illinois
SOURCE: PCT Int. Appl., 406 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039454	A2	20030515	WO 2002-US34324	20021023

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-335952P	P	20011023
US 2001-333545P	P	20011127
US 2002-348464P	P	20020114
US 2002-348615P	P	20020114
US 2002-390804P	P	20020620
US 2002-397557P	P	20020719
US 2002-397619P	P	20020719

OTHER SOURCE(S): MARPAT 138:396233

IT **527676-35-3P**

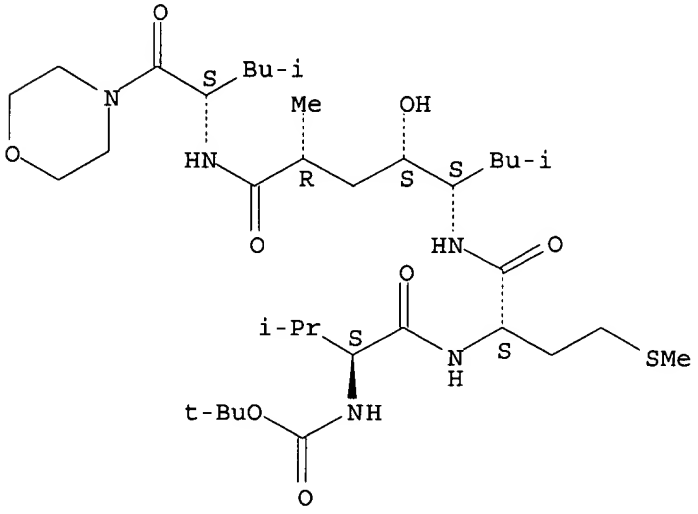
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design of .beta.-secretase inhibitors for treatment of Alzheimer's disease based on crystal structures of .beta.-secretase and side chain interactions in inhibitor complexes)

RN 527676-35-3 CAPLUS

CN L-Methioninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-valyl-N-[(1S,2S,4R)-2-hydroxy-4-methyl-5-[[(1S)-3-methyl-1-(4-morpholinylcarbonyl)butyl]amino]-1-(2-methylpropyl)-5-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB The invention is directed toward substituted hydroxyethylene compds. having the fragment -NHCHR1CH(OH)CH2CHR2CO- [R1 = alkyl, alkylthioalkyl, alkenyl, (hetero)aryl, (hetero)arylalkyl, heterocyclylalkyl, or heterocyclyl; R2 = H, alkyl, cycloalkylalkyl, or (hetero)aryl] for use in treating Alzheimer's disease and similar diseases. In an example, N-[(1S,2S,4R)-1-(3,5-difluorobenzyl)-4-(syn,syn)-(3,5-dimethoxycyclohexylcarbamoyl)-2-hydroxyhexyl]-N,N-dipropylisophathalamide was prepd. by soln.-based methodol.

ACCESSION NUMBER: 2003:43054 CAPLUS
DOCUMENT NUMBER: 138:107007
TITLE: Preparation of 5-amino-4-hydroxypentanoic acid derivatives for treating Alzheimer's disease
INVENTOR(S): Hom, Roy; Mamo, Shumeye; Tung, Jay; Gailunas, Andrea; John, Varghese; Fang, Lawrence
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 113 pp., Cont.-in-part of U. S. Ser. No. 815,960.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003013881	A1	20030116	US 2001-960634	20010921
US 2002019403	A1	20020214	US 2001-816876	20010323
US 2002022623	A1	20020221	US 2001-815960	20010323

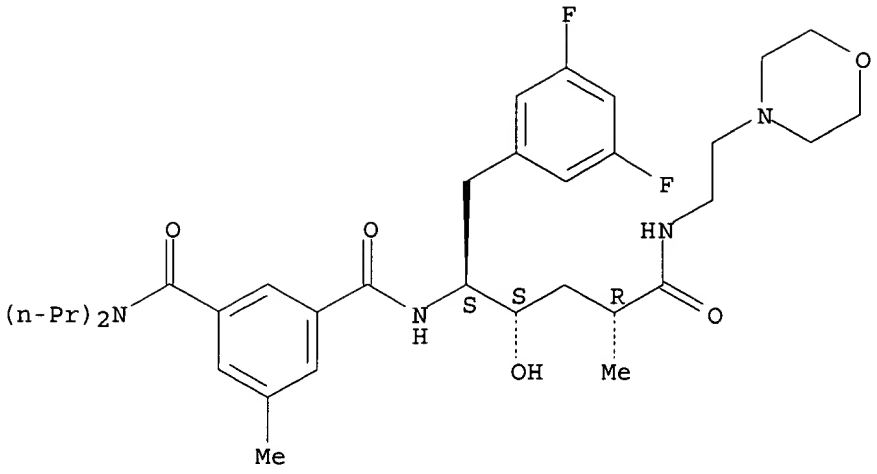
PRIORITY APPLN. INFO.: US 2000-191528P P 20000323
US 2001-815960 A2 20010323
US 2001-816876 A2 20010323
OTHER SOURCE(S): MARPAT 138:107007

IT **362480-29-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino(hydroxy)pentanoic acid derivs. for treating Alzheimer's disease)

RN 362480-29-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2S,4R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-4-methyl-5-[[2-(4-morpholinyl)ethyl]amino]-5-oxopentyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


F
O
N
F
HN
O
O
(n-Pr)2N
N
H
S
S
R
O
OH
Me
Me

L7 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB The prediction of the binding affinity between a protein and ligands is one of the most challenging issues for computational biochem. and drug discovery. While the enthalpic contribution to binding is routinely available with mol. mechanics methods, the entropic contribution is more difficult to est. We describe and apply a relatively simple and intuitive calcn. procedure for estg. the free energy of binding for 53 protein-ligand complexes formed by 17 proteins of known three-dimensional structure and characterized by different active site polarity. HINT, a software model based on exptl. LogPo/w values for small org. mols., was used to evaluate and score all atom-atom hydropathic interactions between the protein and the ligands. These total scores (HTOTAL), which have been previously shown to correlate with .DELTA.Ginteraction for protein-protein interactions, correlate with .DELTA.Gbinding for protein-ligand complexes in the present study with a std. error of .+-.2.6 kcal mol-1 from the equation .DELTA.Gbinding = -0.001 95 HTOTAL - 5.543. A more sophisticated model, utilizing categorized (by interaction class) HINT scores, produces a superior std. error of .+-.1.8 kcal mol-1. It is shown that within families of ligands for the same protein binding site, better models can be obtained with std. errors approaching .+-.1.0 kcal mol-1. Standardized methods for prepg. crystallog. models for hydropathic anal. are also described. Particular attention is paid to the relationship between the ionization state of the ligands and the pH conditions under which the binding measurements are made. Sources and potential remedies of exptl. and modeling errors affecting prediction of .DELTA.Gbinding are discussed.

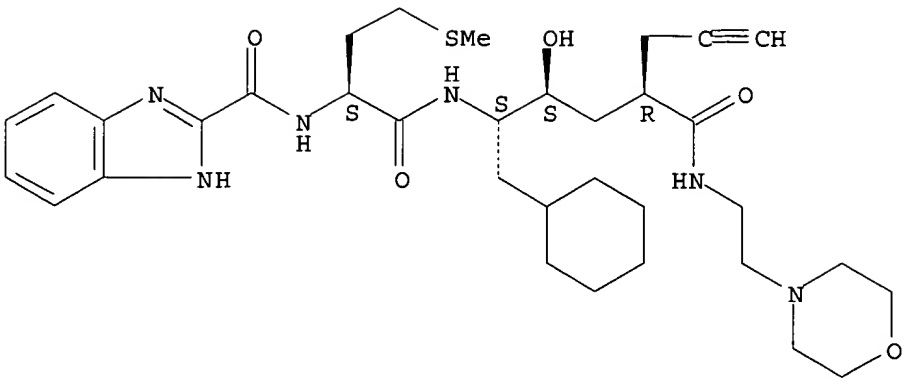
ACCESSION NUMBER: 2002:332765 CAPLUS
DOCUMENT NUMBER: 137:17295
TITLE: Simple, intuitive calculations of free energy of binding for protein-ligand complexes. 1. Models without explicit constrained water
AUTHOR(S): Cozzini, Pietro; Fornabaio, Micaela; Marabotti, Anna; Abraham, Donald J.; Kellogg, Glen E.; Mozzarelli, Andrea
CORPORATE SOURCE: Department of General and Inorganic Chemistry, Department of Biochemistry and Molecular Biology, National Institute for the Physics of Matter, University of Parma, Parma, 43100, Italy
SOURCE: Journal of Medicinal Chemistry (2002), 45(12), 2469-2483
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **433257-54-6**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)
(calcns. of free energy of binding for protein-ligand complexes)

RN 433257-54-6 CAPLUS

CN 1H-Benzimidazole-2-carboxamide, N-[(1S)-1-[[[(1S,2S,4R)-1-(cyclohexylmethyl)-2-hydroxy-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]-6-heptynyl]amino]carbonyl]-3-(methylthio)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB Hydroxyethylenes, such as RNHCHR1CH(OH)CH2CHR2COBR3 [R = peptidyl group, acyl, etc.; R1 = alkyl, alkenyl, arylalkyl, etc.; R2 = H, alkyl, cycloalkyl, arylalkyl, etc.; BR3 = peptidyl group; B = O, NR4; R3 = alkyl, arylalkyl, etc.; R4 = H, alkyl, etc.], were prepd. as agents for the treatment of Alzheimer's disease. Thus, BOC-L-Val-L-Met-NH-(S,S,S)-CH(CH2CHMe2)CH(OH)CH(CHMe2)CO-L-Ala-L-Glu-L-Phe-OH via a series of amide coupling reactions of the corresponding amino acids with the hydroxyethylene moiety. The prepd. hydroxyethylenes were tested for .beta.-secretase inhibiting activity.

ACCESSION NUMBER: 2001:713293 CAPLUS
DOCUMENT NUMBER: 135:273220
TITLE: Preparation of hydroxyethylenes with peptide subunits for pharmaceutical use in the treatment of Alzheimer's disease
INVENTOR(S): Hom, Roy; Mamo, Shumeye; Tung, Jay; Gailunas, Andrea; John, Varghese; Fang, Larry
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 240 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070672	A2	20010927	WO 2001-US9501	20010323
WO 2001070672	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1265849	A2	20021218	EP 2001-926424	20010323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

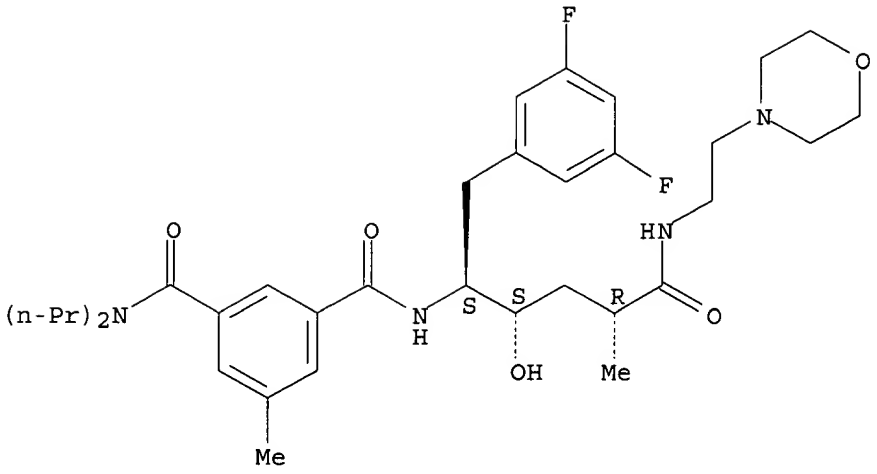
PRIORITY APPLN. INFO.: US 2000-191528P P 20000323
WO 2001-US9501 W 20010323
OTHER SOURCE(S): MARPAT 135:273220

IT **362480-29-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of hydroxyethylenes with peptide subunits for pharmaceutical use in the treatment of Alzheimer's disease)

RN 362480-29-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2S,4R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-4-methyl-5-[[2-(4-morpholinyl)ethyl]amino]-5-oxopentyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


F
O
N
F
HN
O
O
(n-Pr)2N
N
H
S
S
R
O
OH
Me
Me

L7 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB Saccharopepsin is a vacuolar aspartic proteinase involved in activation of a no. of hydrolases. The enzyme has great structural homol. to mammalian aspartic proteinases including human renin and we have used it as a model system to study the binding of renin inhibitors by x-ray crystallog. Five medium-to-high resoln. structures of saccharopepsin complexed with transition-state analog renin inhibitors were detd. The structure of a cyclic peptide inhibitor (PD-129,541) complexed with the proteinase was solved to 2.5 .ANG. resoln. This inhibitor has low affinity for human renin yet binds very tightly to the yeast proteinase (Ki=4 nM). The high affinity of this inhibitor can be attributed to its bulky cyclic moiety spanning P2-P3' and other residues that appear to optimally fit the binding sub-sites of the enzyme. Superposition of the saccharopepsin structure on that of renin showed that a movement of the loop 286-301 relative to renin facilitates tighter binding of this inhibitor to saccharopepsin. Our 2.8 .ANG. resoln. structure of the complex with CP-108,420 shows that its benzimidazole P3 replacement retains one of the std. hydrogen bonds that normally involve the inhibitor's main-chain. This suggests a non-peptide lead in overcoming the problem of susceptible peptide bonds in the design of aspartic proteinase inhibitors. CP-72,647 which possesses a basic histidine residue at P2, has a high affinity for renin (Ki=5 nM) but proves to be a poor inhibitor for saccharopepsin (Ki=3.7 .mu.M). This may stem from the fact that the histidine residue would not bind favorably with the predominantly hydrophobic S2 sub-site of saccharopepsin. (c) 2000 Academic Press.

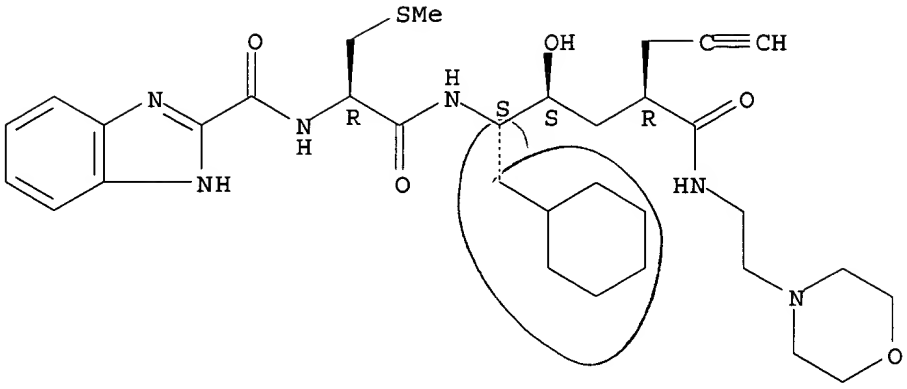
ACCESSION NUMBER: 2000:774937 CAPLUS
DOCUMENT NUMBER: 134:143707
TITLE: X-ray Structures of Five Renin Inhibitors Bound to Saccharopepsin: Exploration of Active-site Specificity
AUTHOR(S): Cronin, Nora B.; Badasso, Mohammed O.; Tickle, Ian J.; Dreyer, Thomas; Hoover, Dennis J.; Rosati, Robert L.; Humblet, Christine C.; Lunney, Elizabeth A.; Cooper, Jonathan B.
CORPORATE SOURCE: Department of Crystallography, Birkbeck College, University of London, London, WC1E 7HX, UK
SOURCE: Journal of Molecular Biology (2000), 303(5), 745-760
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **323576-55-2D**, CP 108420, complexes with saccharopepsin
RL: PRP (Properties)
(X-ray structures of five renin inhibitors bound to saccharopepsin explore active-site specificity of enzyme)

RN 323576-55-2 CAPLUS

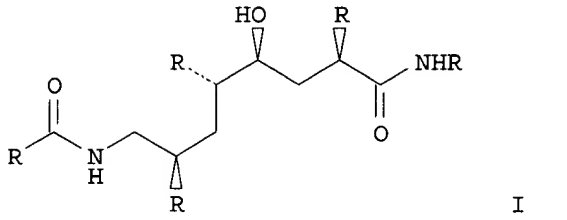
CN 1H-Benzimidazole-2-carboxamide, N-[(1R)-2-[[(1S,2S,4R)-1-(cyclohexylmethyl)-2-hydroxy-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]-6-heptynyl]amino]-1-[(methylthio)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

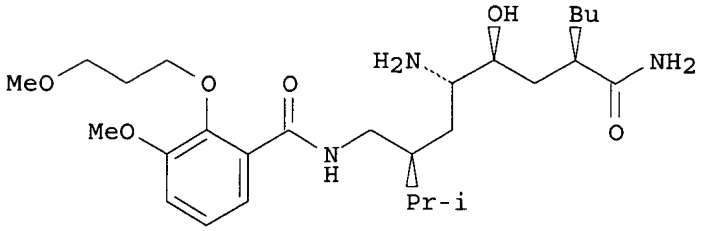


REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I



II

AB The N-[amino(hydroxy)oxooctyl]amides I (R1 = aryl; R2 = aliph. group; R3 = aminoalkyl group; R5 = alkyl, cycloalkyl, etc.; X1, X2 = methylene, carbonyl) were disclosed. I are useful as renin inhibitors and for the treatment of hypertension. A claimed example compd. is (2S,4S,5S,7R)-N-(4-amino-7-butyl-7-carbamoyl-5-hydroxy-2-isopropyloctyl)-3-methoxy-2-(3-methoxypropoxy)benzamide (II).

ACCESSION NUMBER: 1996:501390 CAPLUS
DOCUMENT NUMBER: 125:167576
TITLE: Aryl-substituted .omega.-aminoalkanamides and diamides and their use as renin inhibitors
INVENTOR(S): Maibaum, Juergen K.; Rigollier, Pascal; Herold, Peter; Cohen, Nissim C.; Goeschke, Richard; Stutz, Stefan
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 90 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 716077	A1	19960612	EP 1995-810743	19951129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
FI 9505836	A	19960609	FI 1995-5836	19951204
CA 2164571	AA	19960609	CA 1995-2164571	19951206
ZA 9510354	A	19960610	ZA 1995-10354	19951206
AU 9540266	A1	19960613	AU 1995-40266	19951206
US 5641778	A	19970624	US 1995-568332	19951206
NO 9504975	A	19960610	NO 1995-4975	19951207
JP 08231485	A2	19960910	JP 1995-319220	19951207
CN 1136556	A	19961127	CN 1995-113102	19951207
HU 74454	A2	19961230	HU 1995-3508	19951207

PRIORITY APPLN. INFO.: CH 1994-3724 19941208

OTHER SOURCE(S): MARPAT 125:167576

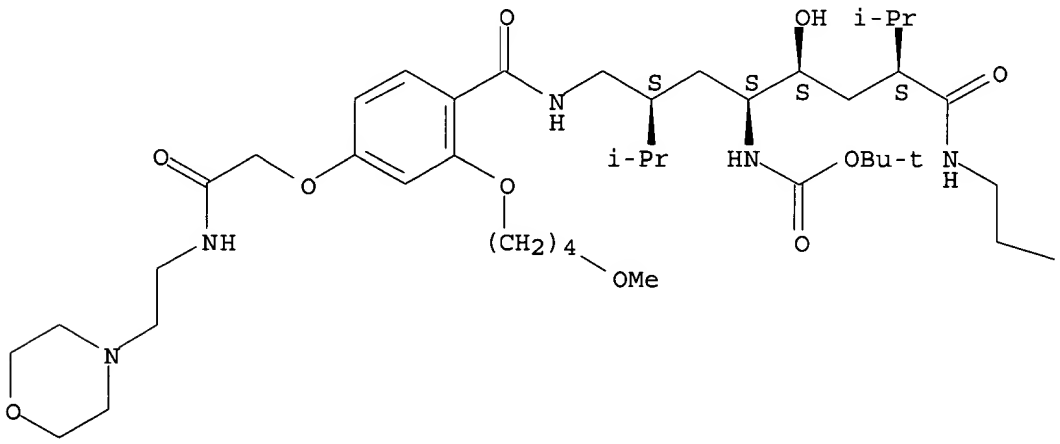
IT **179995-48-3P 179995-61-0P 179995-62-1P**
179995-63-2P 179995-64-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-[amino(hydroxy)oxooctyl]amides as renin inhibitors)

RN 179995-48-3 CAPLUS

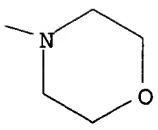
CN Carbamic acid, [2-hydroxy-1-[2-[[[2-(4-methoxybutoxy)-4-[2-[[2-(4-morpholinyl)ethyl]amino]-2-oxoethoxy]benzoyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



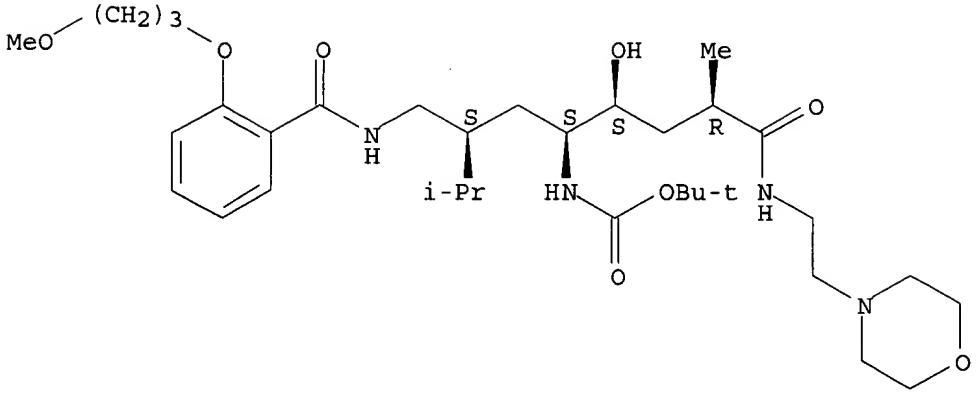
PAGE 1-B



RN 179995-61-0 CAPLUS

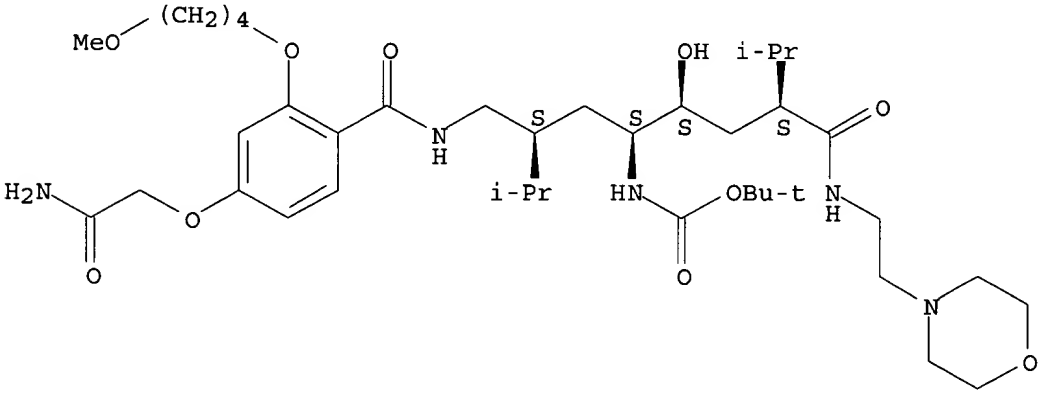
CN Carbamic acid, [2-hydroxy-1-[2-[[[2-(3-methoxypropoxy)benzoyl]amino]methyl]-3-methylbutyl]-4-methyl-5-[[2-(4-morpholinyl)ethyl]amino]-5-oxopentyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



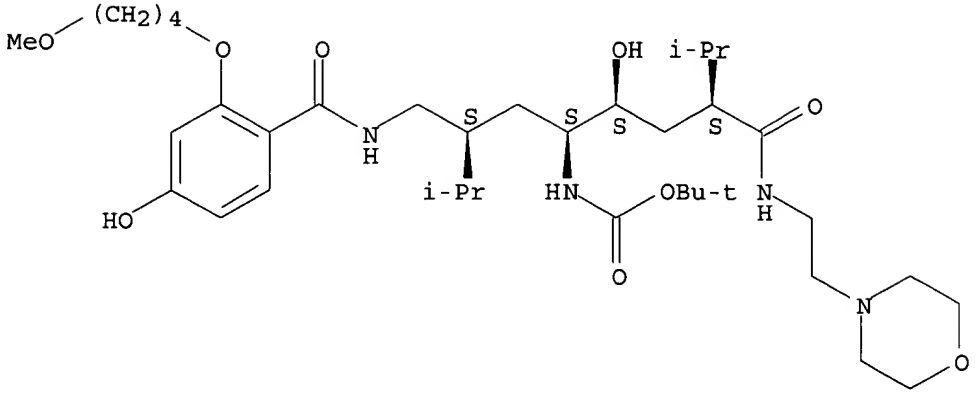
RN 179995-62-1 CAPLUS
CN Carbamic acid, [1-[2-[[[4-(2-amino-2-oxoethoxy)-2-(4-methoxybutoxy)benzoyl]amino]methyl]-3-methylbutyl]-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



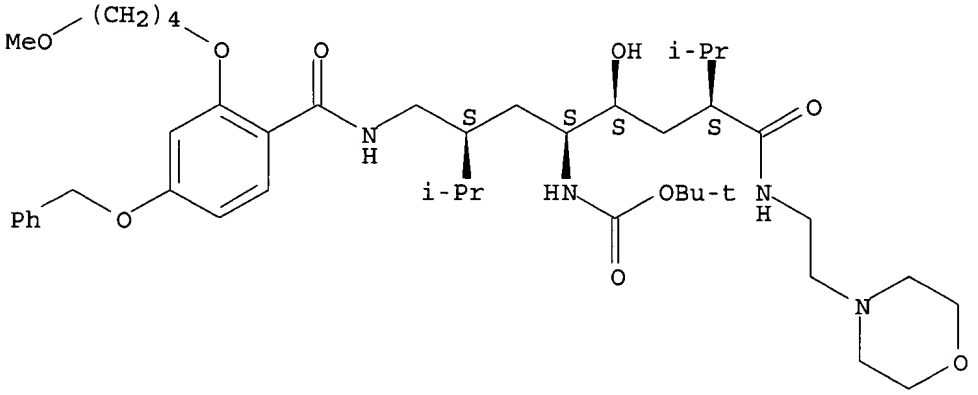
RN 179995-63-2 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[4-hydroxy-2-(4-methoxybutoxy)benzoyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



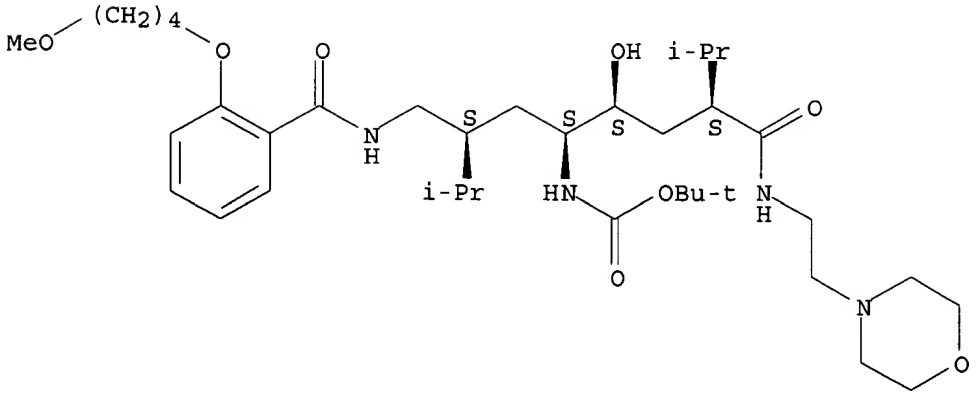
RN 179995-64-3 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[2-(4-methoxybutoxy)-4-(phenylmethoxy)benzoyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



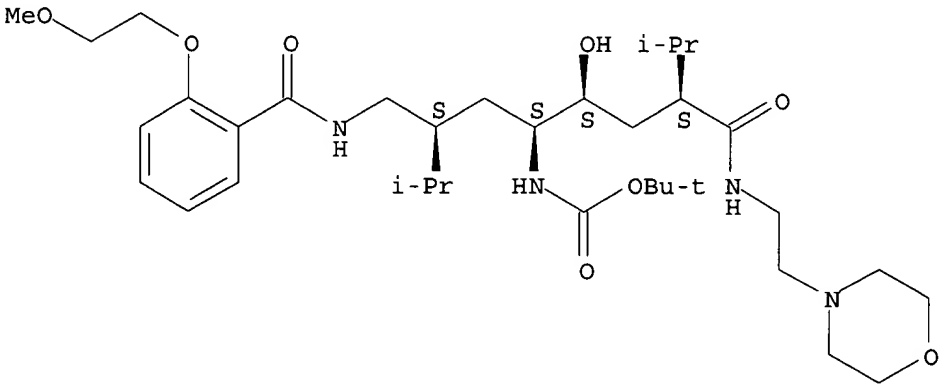
IT **179993-71-6P 179993-72-7P 179993-73-8P**
179993-74-9P 179993-75-0P 179993-76-1P
179993-77-2P 179993-80-7P 179993-81-8P
179993-82-9P 179993-83-0P 179993-84-1P
179993-85-2P 179993-86-3P 179995-94-9P
179995-95-0P 179995-99-4P 180183-22-6P
180183-23-7P 180183-25-9P 180183-26-0P
180183-27-1P 180183-28-2P 180183-29-3P
180183-44-2P 180183-57-7P 180183-58-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-[amino(hydroxy)oxooctyl]amides as renin inhibitors)
RN 179993-71-6 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[2-(4-methoxybutoxy)benzoyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



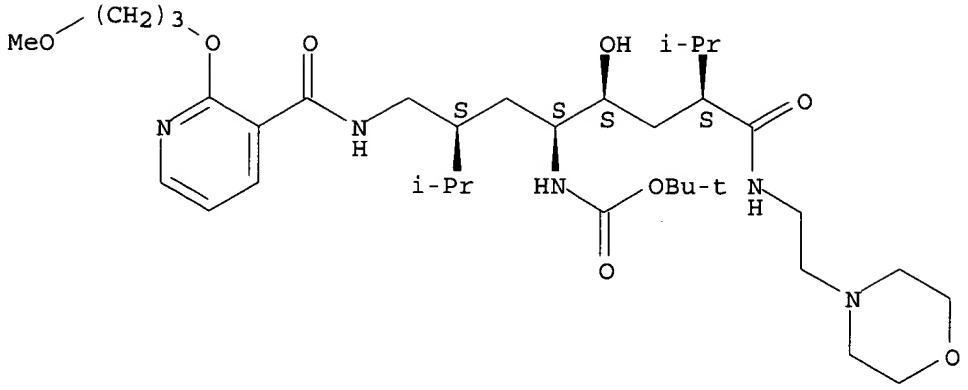
RN 179993-72-7 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[2-(2-methoxyethoxy)benzoyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



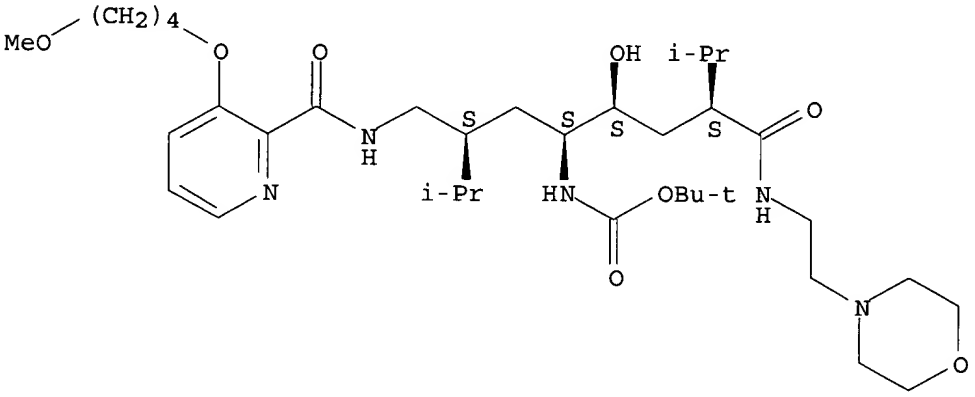
RN 179993-73-8 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[[2-(3-methoxypropoxy)-3-pyridinyl]carbonyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



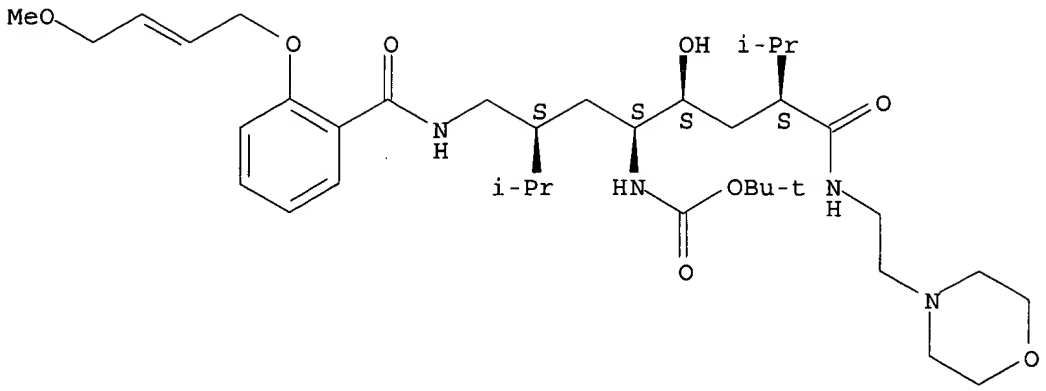
RN 179993-74-9 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[[3-(4-methoxybutoxy)-2-pyridinyl]carbonyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



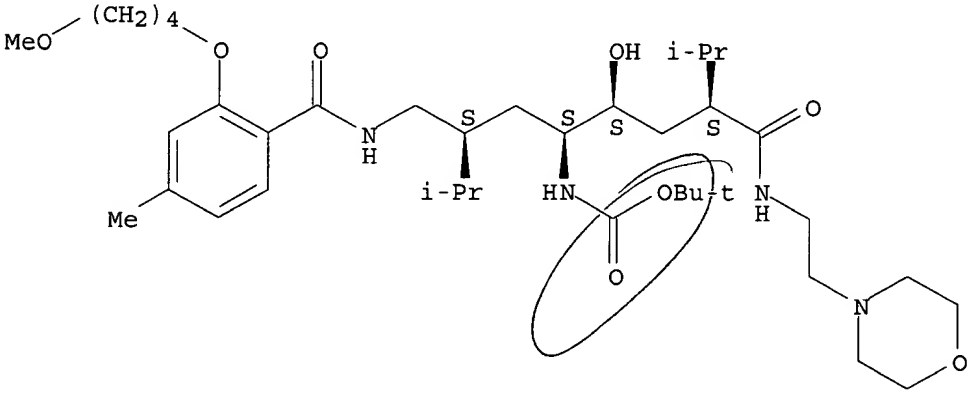
RN 179993-75-0 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[2-[(4-methoxy-2-butenyl)oxy]benzoyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(2R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



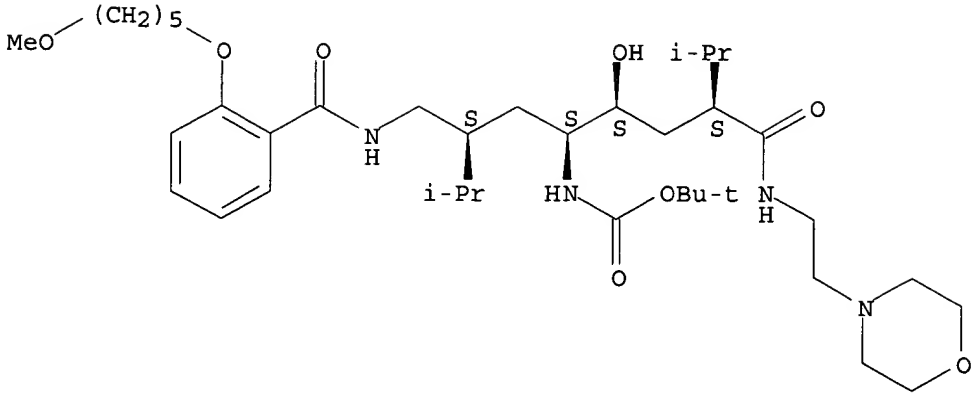
RN 179993-76-1 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[2-(4-methoxybutoxy)-4-methylbenzoyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



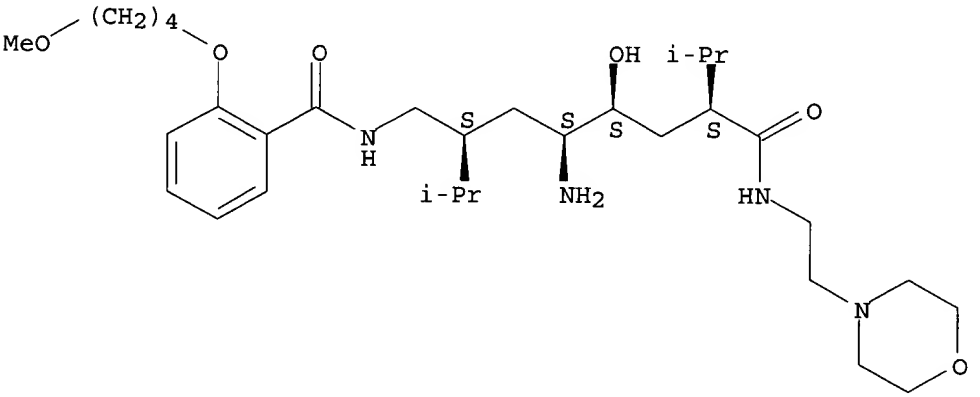
RN 179993-77-2 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[[2-[(5-methoxypentyl)oxy]benzoyl]amino]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 179993-80-7 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(4-methoxybutoxy)-, dihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

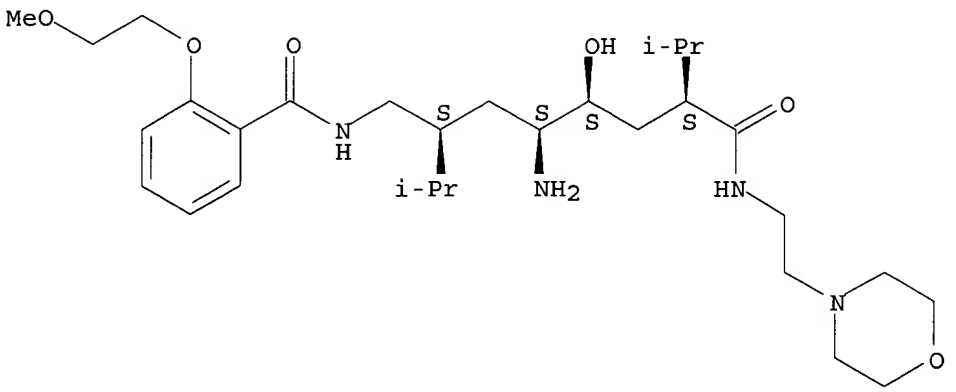
Absolute stereochemistry.



●2 HCl

RN 179993-81-8 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(2-methoxyethoxy)-, dihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

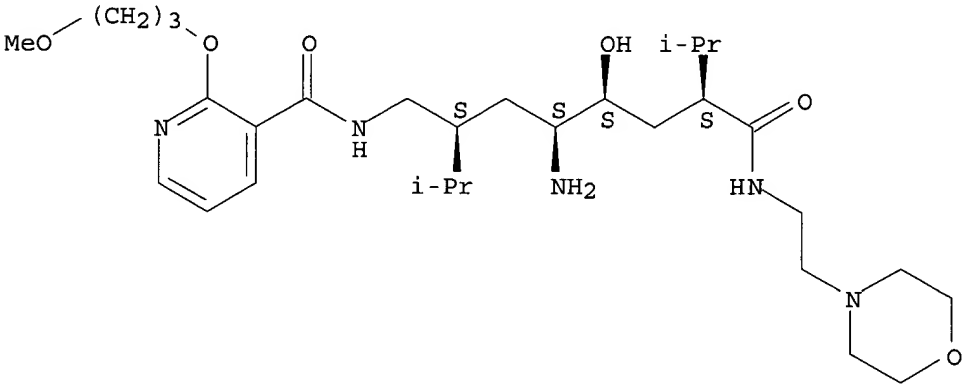
Absolute stereochemistry.



●2 HCl

RN 179993-82-9 CAPLUS
CN 3-Pyridinecarboxamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(3-methoxypropoxy)-, dihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

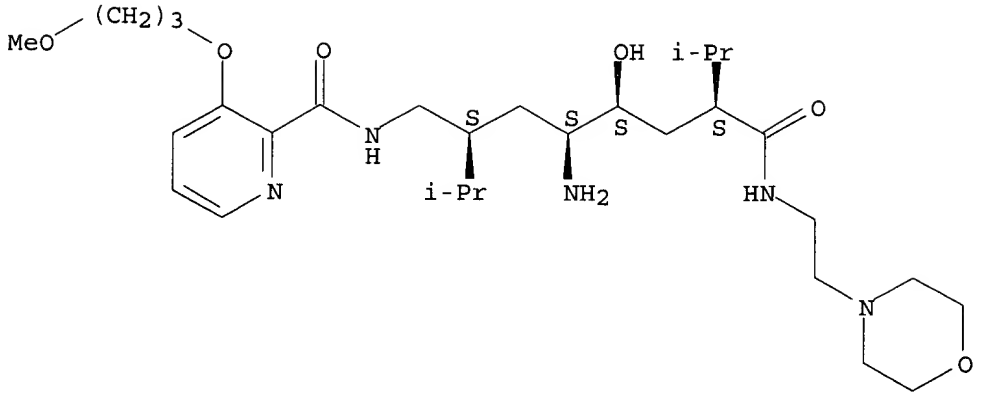
Absolute stereochemistry.



●2 HCl

RN 179993-83-0 CAPLUS
CN 2-Pyridinecarboxamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-3-(3-methoxypropoxy)-, dihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

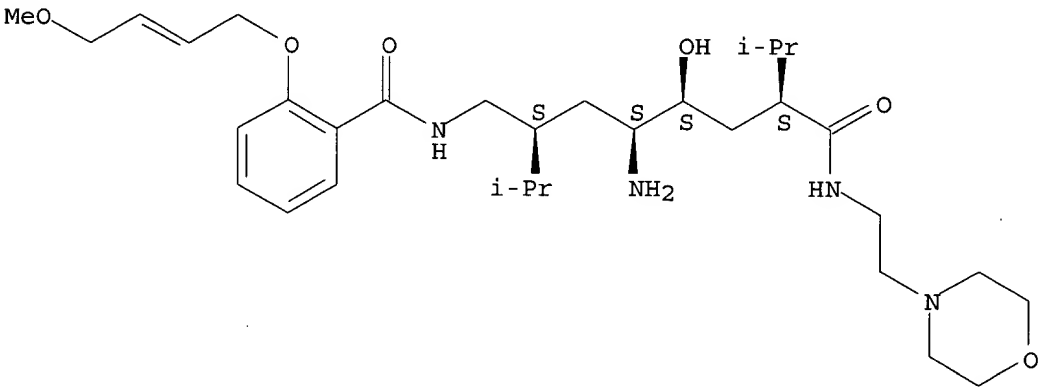
Absolute stereochemistry.



●2 HCl

RN 179993-84-1 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-[(4-methoxy-2-butenyl)oxy]-, dihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

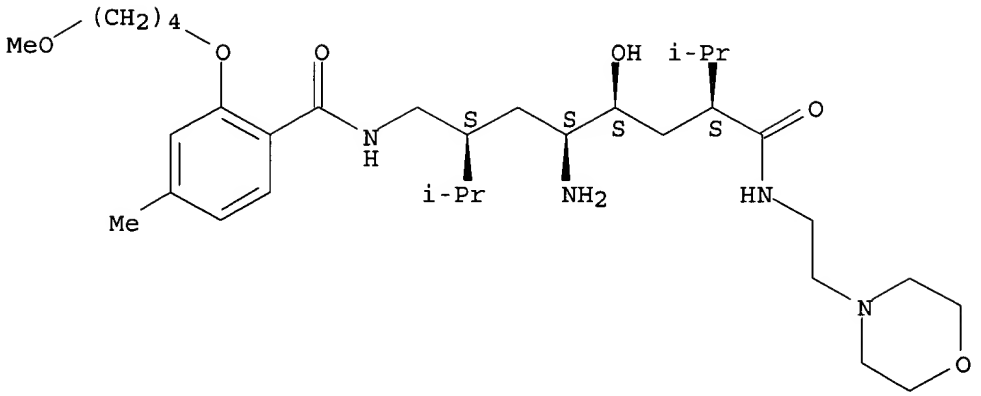
Absolute stereochemistry.
Double bond geometry unknown.



●2 HCl

RN 179993-85-2 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(4-methoxybutoxy)-4-methyl-, dihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

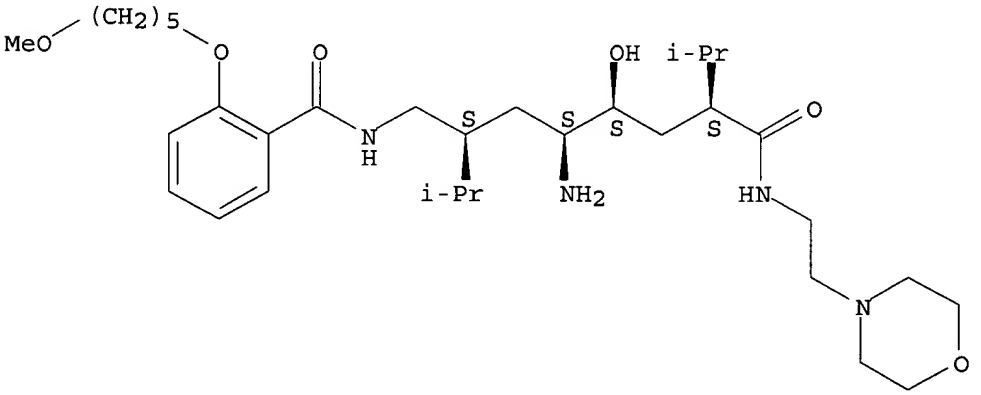
Absolute stereochemistry.



●2 HCl

RN 179993-86-3 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-[(5-methoxypentyl)oxy]-, dihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

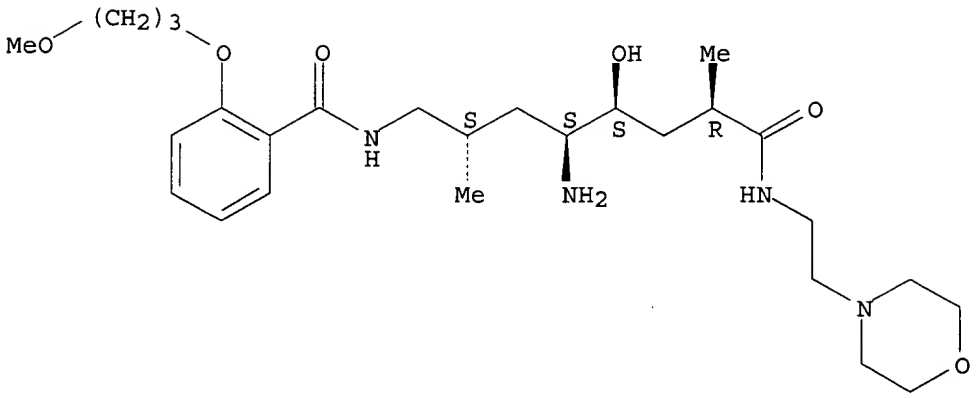
Absolute stereochemistry.



●2 HCl

RN 179995-94-9 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-2,7-dimethyl-8-[[2-(4-morpholinyl)ethyl]amino]-8-oxooctyl]-2-(3-methoxypropoxy)-, dihydrochloride, [2S-(2R*,4R*,5R*,7S*)]- (9CI) (CA INDEX NAME)

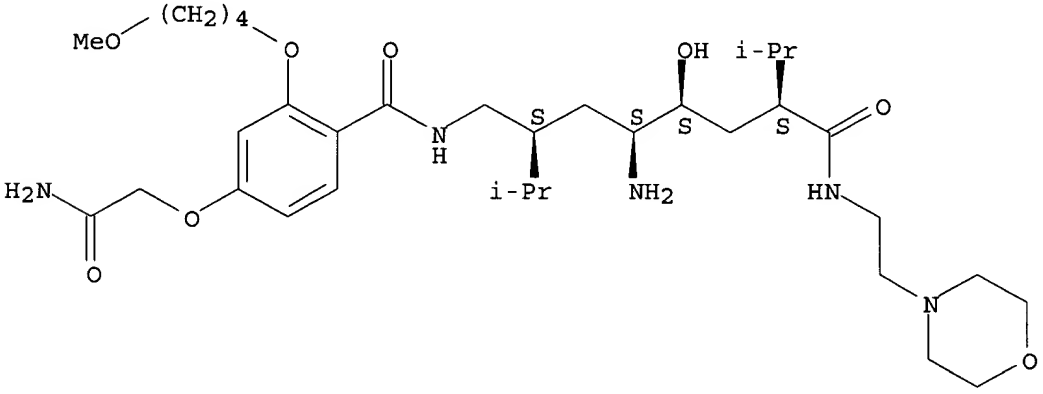
Absolute stereochemistry.



●2 HCl

RN 179995-95-0 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-4-(2-amino-2-oxoethoxy)-2-(4-methoxybutoxy)-, dihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

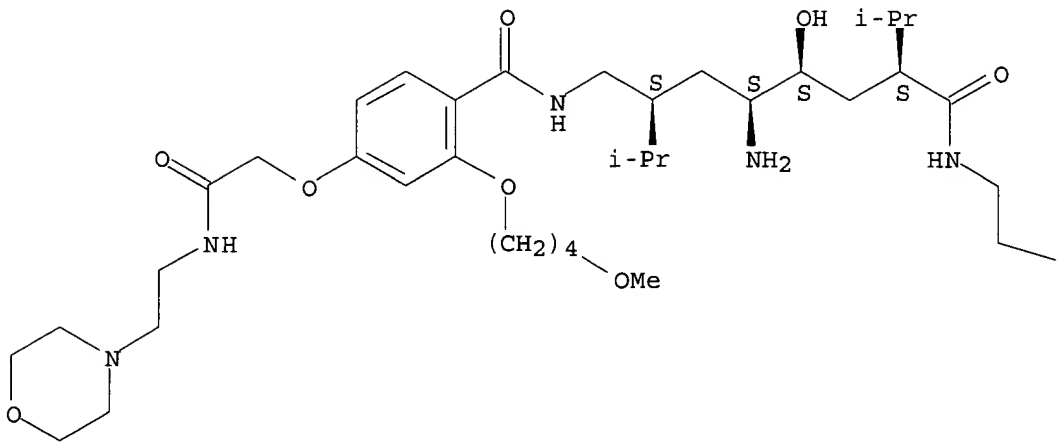


●2 HCl

RN 179995-99-4 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(4-methoxybutoxy)-4-[2-[[2-(4-morpholinyl)ethyl]amino]-2-oxoethoxy]-, trihydrochloride, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

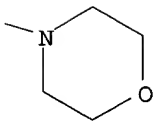
Absolute stereochemistry.

PAGE 1-A



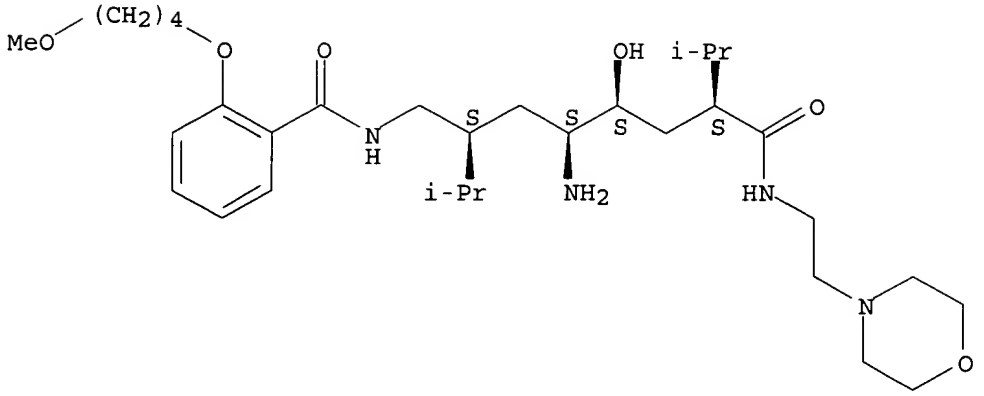
● 3 HCl

PAGE 1-B



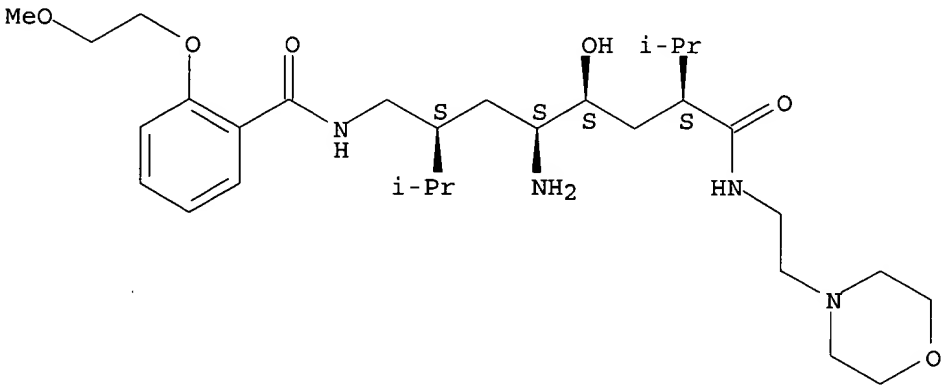
RN 180183-22-6 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(4-methoxybutoxy)-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



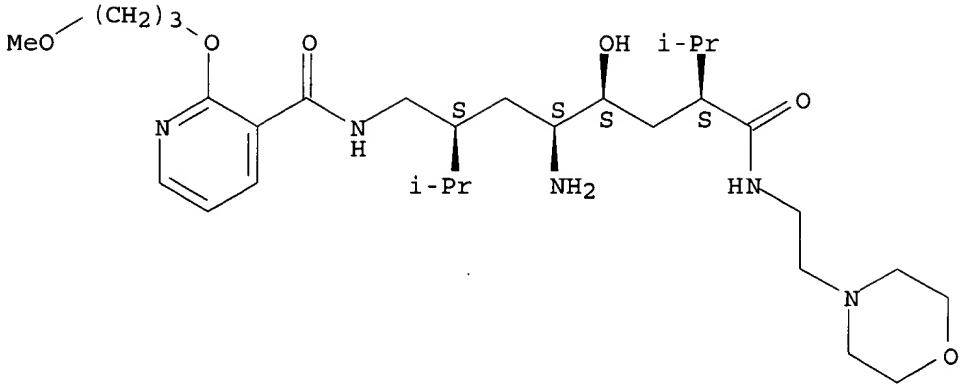
RN 180183-23-7 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(2-methoxyethoxy)-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



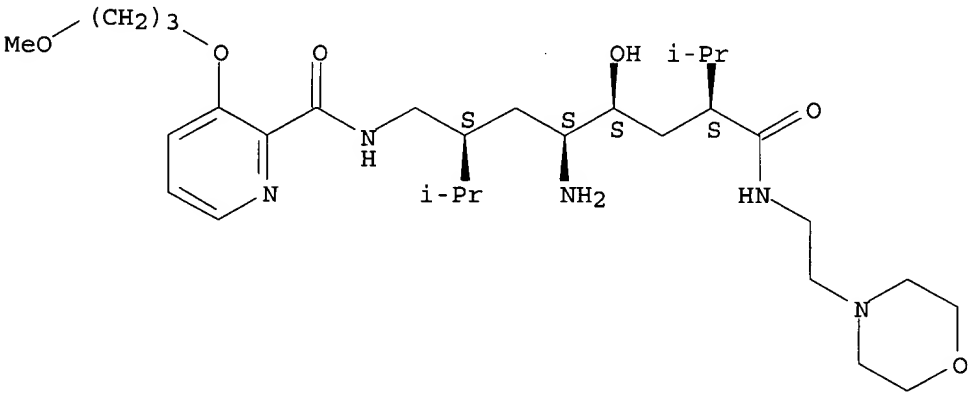
RN 180183-25-9 CAPLUS
CN 3-Pyridinecarboxamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(3-methoxypropoxy)-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



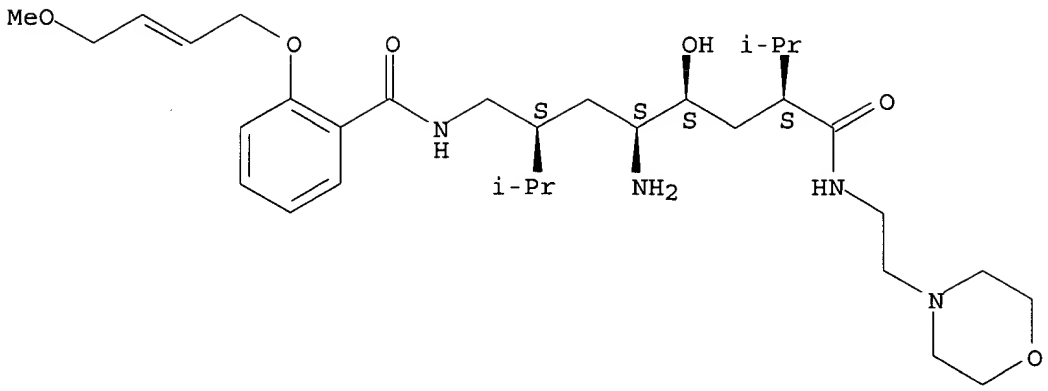
RN 180183-26-0 CAPLUS
CN 2-Pyridinecarboxamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-3-(3-methoxypropoxy)-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



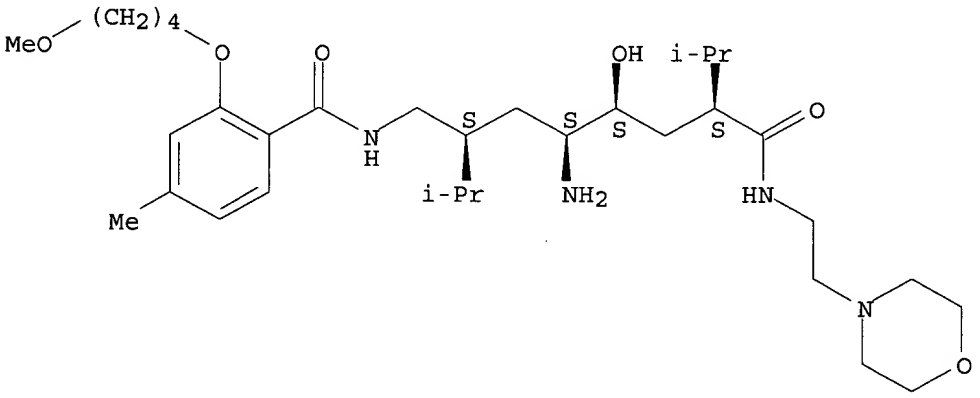
RN 180183-27-1 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-[(4-methoxy-2-butenyl)oxy]-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



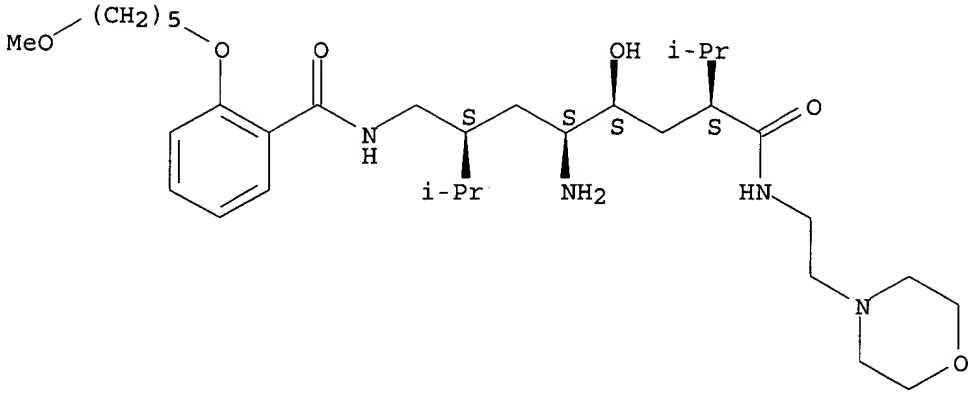
RN 180183-28-2 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(4-methoxybutoxy)-4-methyl-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180183-29-3 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-[(5-methoxypentyl)oxy]-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

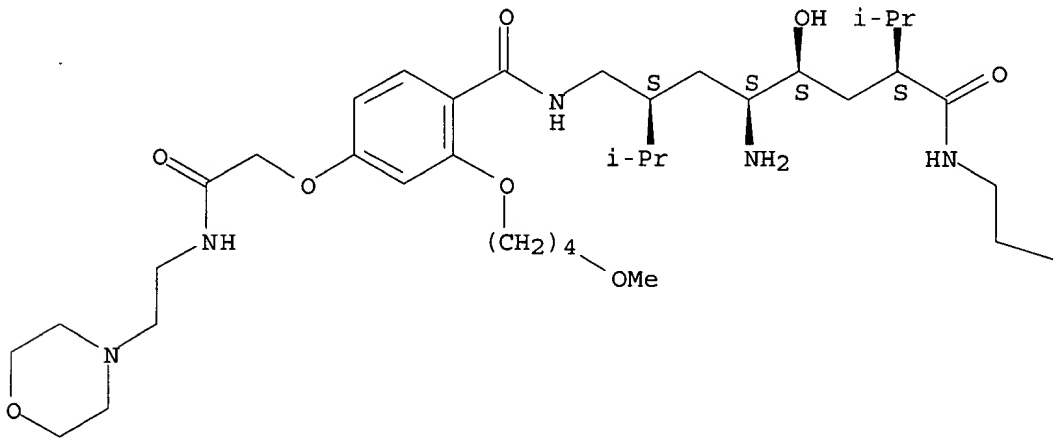
Absolute stereochemistry.

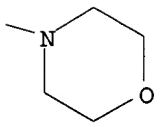


RN 180183-44-2 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-2-(4-methoxybutoxy)-4-[2-[[2-(4-morpholinyl)ethyl]amino]-2-oxoethoxy]-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

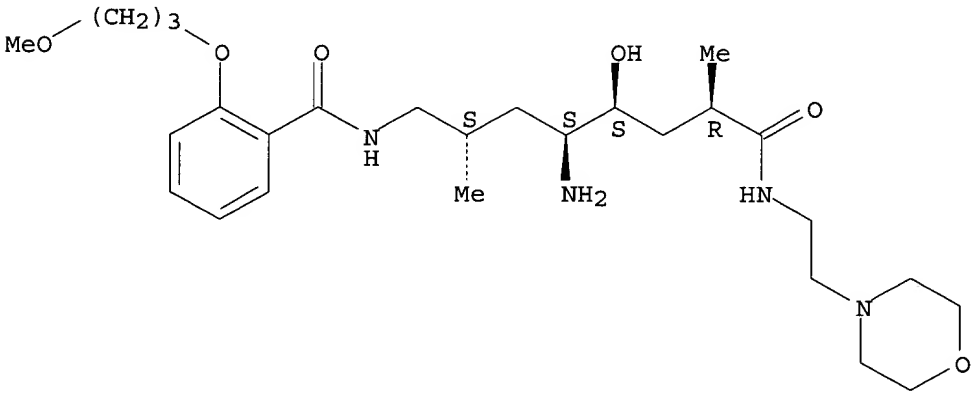
PAGE 1-A





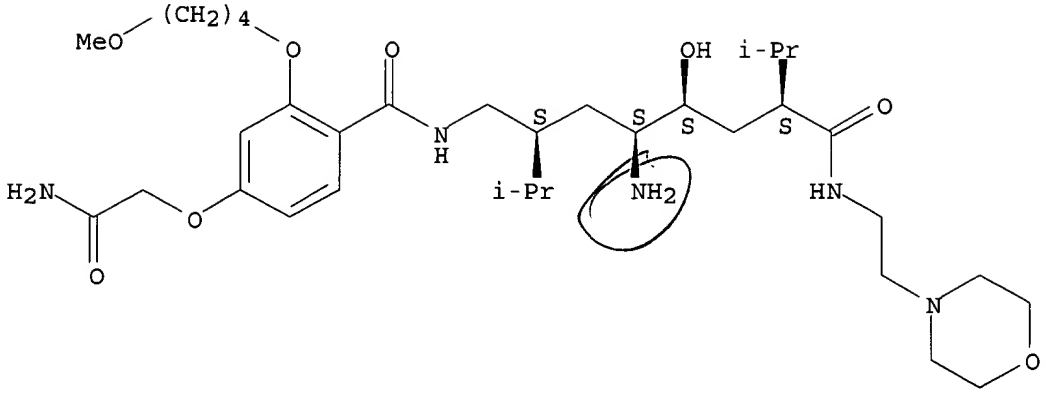
RN 180183-57-7 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-2,7-dimethyl-8-[[2-(4-morpholinyl)ethyl]amino]-8-oxooctyl]-2-(3-methoxypropoxy)-, [2S-(2R*,4R*,5R*,7S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180183-58-8 CAPLUS
CN Benzamide, N-[4-amino-5-hydroxy-8-methyl-2-(1-methylethyl)-7-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]nonyl]-4-(2-amino-2-oxoethoxy)-2-(4-methoxybutoxy)-, [2S-(2R*,4R*,5R*,7R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB R1XCH2CR2R3CH2CH(NHR4)CHR5CH2CR6R7CONHR8 [I; R1 = arylamino, N-aryl-N-aralkylamino, N-attached heterocyclyl, etc.; R3,R3,R7 = H or alkyl; R2R3 = alkylene; R4 = H, alkyl, alkanoyl, alkoxycarbonyl; R5 = OH, alkanoyloxy, alkoxycarbonyloxy; R6 = H, (ar)alkyl, alkenyl, etc.; R6R7 = alkylene; R8 = (cyclo)aliph. group, heteroaliph. group; X = CO or CH2] were prepd. Thus, quinoline-3-carboxylic acid was converted in 21 steps to N-butyl-(2R,4S,5S)-5-amino-4-hydroxy-2,7,7-trimethyl-8-(3RS-methoxycarbonyl-1,2,3,4-tetrahydroquinolin-1-carbonyl)octanamide. I gave inhibition of human renin at .apprx.10-6 to .apprx.10-10M in vitro.

ACCESSION NUMBER: 1996:335954 CAPLUS
DOCUMENT NUMBER: 125:10631
TITLE: Preparation of 2,9-diamino- and 2-amino-8-carbamoyl-4-hydroxyalkanoic acid amides as renin inhibitors
INVENTOR(S): Rasetti, Vittorio; Rueeger, Heinrich; Maibaum, Juergen Klaus; Mah, Robert; Gruetter, Markus; Cohen, Nissim Claude
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 115 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

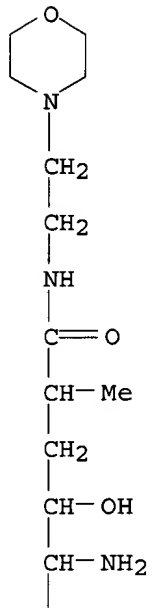
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 702004	A2	19960320	EP 1995-113964	19950906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AU 9530534	A1	19960328	AU 1995-30534	19950908
US 5719141	A	19980217	US 1995-525254	19950908
FI 9504255	A	19960316	FI 1995-4255	19950911
CA 2158227	AA	19960316	CA 1995-2158227	19950913
ZA 9507726	A	19960315	ZA 1995-7726	19950914
NO 9503629	A	19960318	NO 1995-3629	19950914
HU 74453	A2	19961230	HU 1995-2684	19950914
CN 1169986	A	19980114	CN 1995-118418	19950914
JP 08176087	A2	19960709	JP 1995-238779	19950918

PRIORITY APPLN. INFO.: CH 1994-2816 19940915
OTHER SOURCE(S): MARPAT 125:10631

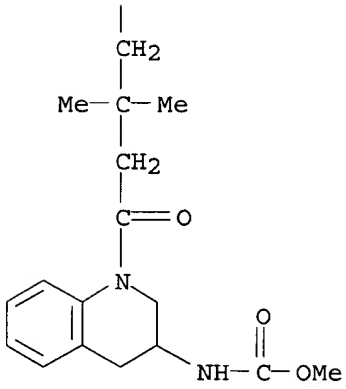
IT **177198-20-8P 177198-22-0P 177198-24-2P**
177198-26-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,9-diamino- and 2-amino-8-carbamoyl-4-hydroxyalkanoic acid amides as renin inhibitors)

RN 177198-20-8 CAPLUS
CN Carbamic acid, [1-[5-amino-6-hydroxy-3,3,8-trimethyl-9-[[2-(4-morpholinyl)ethyl]amino]-1,9-dioxononyl]-1,2,3,4-tetrahydro-3-quinolinyl]-, methyl ester, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



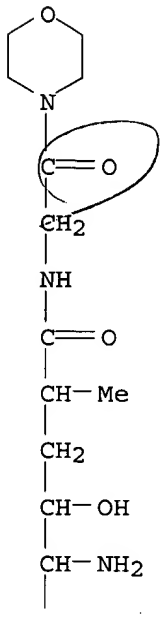
PAGE 2-A



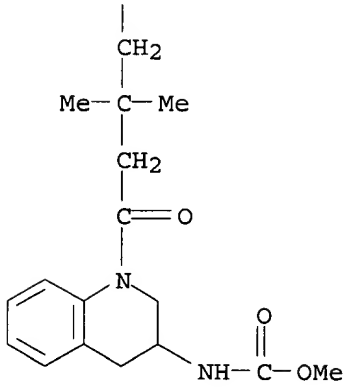
●2 HCl

RN 177198-22-0 CAPLUS
CN Carbamic acid, [1-[5-amino-6-hydroxy-3,3,8-trimethyl-9-[[2-(4-morpholinyl)-2-oxoethyl]amino]-1,9-dioxononyl]-1,2,3,4-tetrahydro-3-quinolinyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



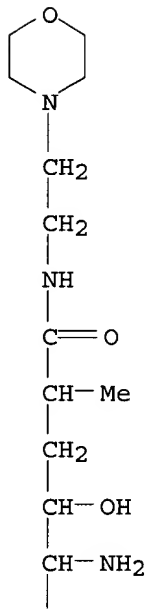
PAGE 2-A



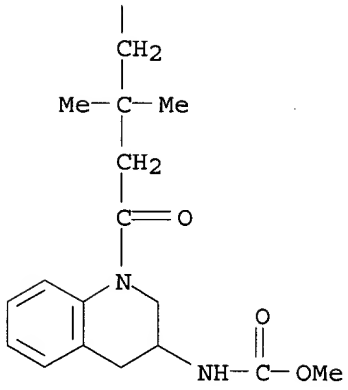
● HCl

RN 177198-24-2 CAPLUS
CN Carbamic acid, [1-[5-amino-6-hydroxy-3,3,8-trimethyl-9-[[2-(4-morpholinyl)ethyl]amino]-1,9-dioxononyl]-1,2,3,4-tetrahydro-3-quinolinyl]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

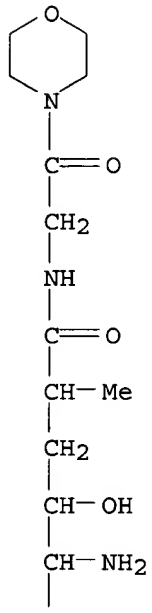


PAGE 2-A

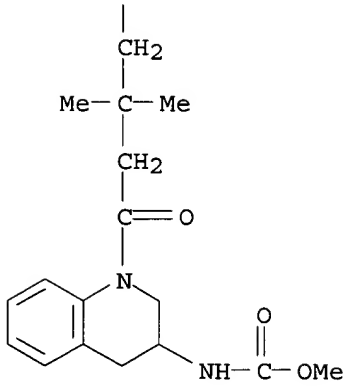


RN 177198-26-4 CAPLUS
CN Carbamic acid, [1-[5-amino-6-hydroxy-3,3,8-trimethyl-9-[[2-(4-morpholinyl)-2-oxoethyl]amino]-1,9-dioxononyl]-1,2,3,4-tetrahydro-3-quinolinyl]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

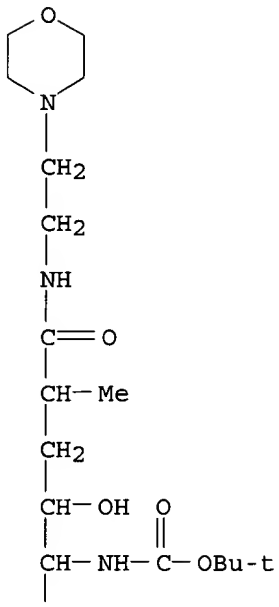


IT **177202-55-0P 177202-58-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 2,9-diamino- and 2-amino-8-carbamoyl-4-hydroxyalkanoic acid amides as renin inhibitors)

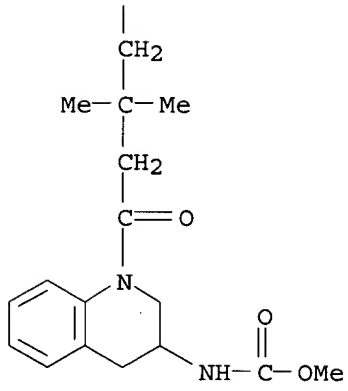
RN 177202-55-0 CAPLUS

CN Carbamic acid, [1-[4-[3,4-dihydro-3-[(methoxycarbonyl)amino]-1(2H)-quinolinyl]-2,2-dimethyl-4-oxobutyl]-2-hydroxy-4-methyl-5-[[2-(4-morpholinyl)ethyl]amino]-5-oxopentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

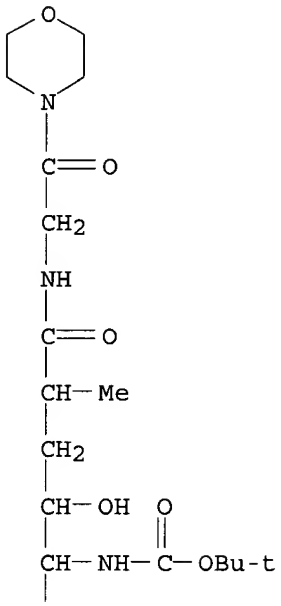


PAGE 2-A

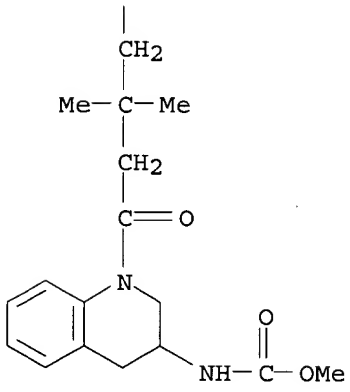


RN 177202-58-3 CAPLUS
CN Carbamic acid, [1-[4-[3,4-dihydro-3-[(methoxycarbonyl)amino]-1(2H)-quinolinyl]-2,2-dimethyl-4-oxobutyl]-2-hydroxy-4-methyl-5-[[2-(4-morpholinyl)-2-oxoethyl]amino]-5-oxopentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

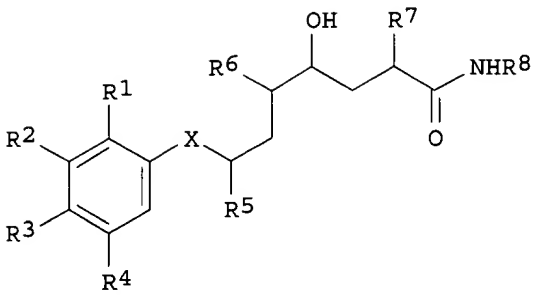
PAGE 1-A



PAGE 2-A



L7 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I

AB Title compds. [I; R1 = H, OH, alkoxy, cycloalkoxy, alkoxyalkoxy, (amidated or esterified) CO2H; R2 = H, alkyl, cylcoalkyl, alkoxyalkyl, cycloalkoxyalkyl, OH, hydroxyalkoxy, heteroarylalkyl, etc.; R3 = (halogenated) alkyl, alkoxyalkyl, hydroxyalkyl, (S-oxidized) alkylthioalkyl, etc.; R4 = H, alkyl, OH, alkoxy, cycloalkoxy; R3R4 = alkylenedioxy, condensed benzo- or cyclohexeno ring; X = CH2, CHOH; R5 = alkyl, cycloalkyl; R6 = (alkylated alkanoylated) amino; R7 = alkyl, alkenyl, cycloalkyl, aralkyl; R8 = alkyl, cycloalkyl, (esterified or etherified) hydroxyalkyl, (esterified or amidated) carboxyalkyl, etc.], were prepd. Thus, 2(R,S)-methyl-4(S)-hydroxy-5(S)-amino-7(S)-isopropyl-8-(p-tert-butylphenyl)octanoic acid N-butylamide hydrochloride was prepd. in several steps starting with 3-isovaleryl-4(R)-benzyloxazolidin-2-one and p-tert-butylbenzyl bromide. I inhibited human plasma renin with IC50 = 10-6-10-10 M, and reduced blood pressure in marmosets at 0.003-0.3 mg/kg i.v.

ACCESSION NUMBER: 1995:995373 CAPLUS
DOCUMENT NUMBER: 124:201791
TITLE: Preparation of .delta.-amino-.gamma.-hydroxy-.omega.-arylalkanoic acid amides as renin inhibitors.
INVENTOR(S): Goeschke, Richard; Maibaum, Juergen Klaus; Schilling, Walter; Stutz, Stefan; Rigollier, Pascal; Yamaguchi, Yasuchika; Cohen, Nissim Claude; Herold, Peter
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 115 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 678503	A1	19951025	EP 1995-810236	19950407
EP 678503	B1	19990901		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5559111	A	19960924	US 1995-416242	19950404
AT 183997	E	19990915	AT 1995-810236	19950407
ES 2137478	T3	19991216	ES 1995-810236	19950407
FI 9501771	A	19951019	FI 1995-1771	19950412
NO 9501441	A	19951019	NO 1995-1441	19950412
AU 9516421	A1	19951026	AU 1995-16421	19950412

AU 699616	B2	19981210			
ZA 9503051	A	19951018	ZA 1995-3051		19950413
ZA 9503052	A	19951018	ZA 1995-3052		19950413
CA 2147056	AA	19951019	CA 1995-2147056		19950413
ZA 9503050	A	19951108	ZA 1995-3050		19950413
HU 71701	A2	19960129	HU 1995-1078		19950414
HU 74074	A2	19961028	HU 1995-1076		19950414
CZ 287935	B6	20010314	CZ 1995-976		19950414
TW 402582	B	20000821	TW 1995-84103732		19950415
CN 1117960	A	19960306	CN 1995-105037		19950417
IL 113403	A1	20010724	IL 1995-113403		19950417
JP 08081430	A2	19960326	JP 1995-92532		19950418
JP 3240322	B2	20011217			
US 5654445	A	19970805	US 1996-674555		19960702
US 5627182	A	19970506	US 1996-687878		19960725
US 5646143	A	19970708	US 1996-687277		19960725
US 5705658	A	19980106	US 1997-800671		19970214

PRIORITY APPLN. INFO.:

CH 1994-1169	A	19940418
US 1995-416242	A3	19950404
US 1996-687277	A3	19960725

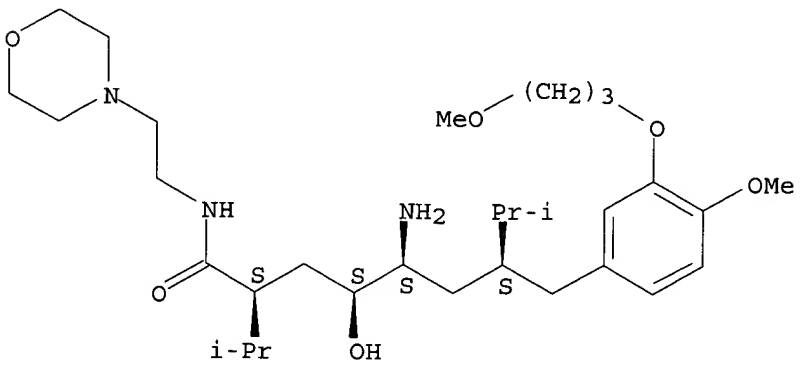
OTHER SOURCE(S): MARPAT 124:201791

IT **172900-85-5P 173154-15-9P 173334-59-3P**
173334-61-7P 173334-62-8P 173334-73-1P
173334-85-5P 173335-00-7P 173335-02-9P
173335-03-0P 173335-48-3P 173335-58-5P
173335-60-9P 173335-62-1P 173335-64-3P
173335-66-5P 173399-02-5P 173399-13-8P
173399-24-1P 173399-85-4P 173399-86-5P
173399-96-7P 173400-32-3P 173521-34-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .delta.-amino-.gamma.-hydroxy-.omega.-arylalkanoic acid amides as renin inhibitors)

RN 172900-85-5 CAPLUS

CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, dihydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

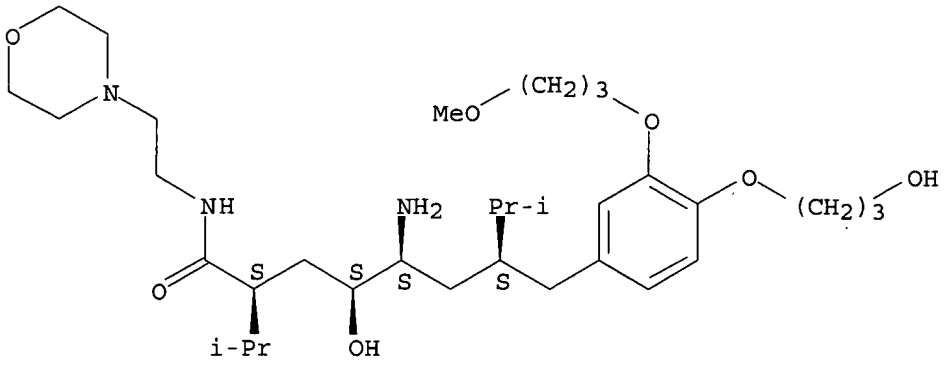
Absolute stereochemistry.



●2 HCl

RN 173154-15-9 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-(3-hydroxypropoxy)-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, monohydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

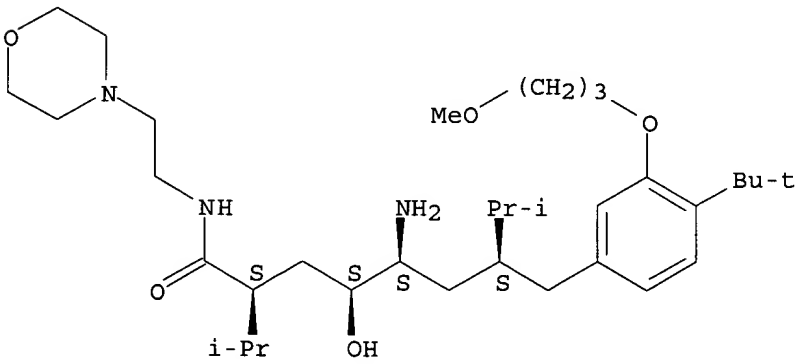
Absolute stereochemistry.



● HCl

RN 173334-59-3 CAPLUS
CN Benzeneoctanamide, .delta.-amino-4-(1,1-dimethylethyl)-.gamma.-hydroxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, dihydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

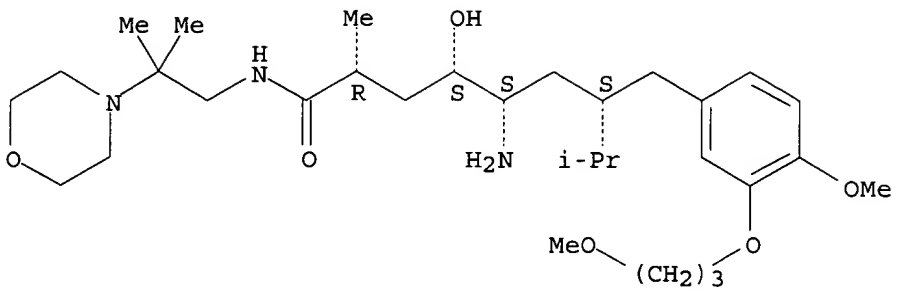
Absolute stereochemistry.



●2 HCl

RN 173334-61-7 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.-methyl-.zeta.-(1-methylethyl)-N-[2-methyl-2-(4-morpholinyl)propyl]-, dihydrochloride, [.alpha.R-(.alpha.R*,.gamma.S*,.delta.S*,.zeta.S*)]- (9CI) (CA INDEX NAME)

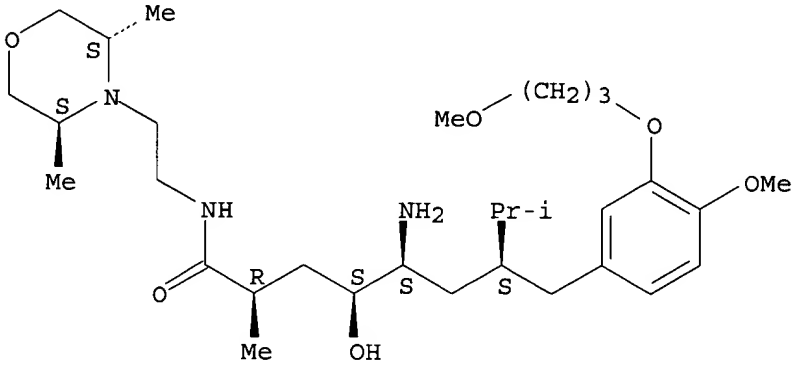
Absolute stereochemistry.



●2 HCl

RN 173334-62-8 CAPLUS
CN Benzeneoctanamide, .delta.-amino-N-[2-(3,5-dimethyl-4-morpholinyl)ethyl]-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.-methyl-.zeta.-(1-methylethyl)-, dihydrochloride, [3S-[3.alpha.,4(.alpha.S*,.gamma.R*,.delta.R*,.zeta.R*),5.beta.]]- (9CI) (CA INDEX NAME)

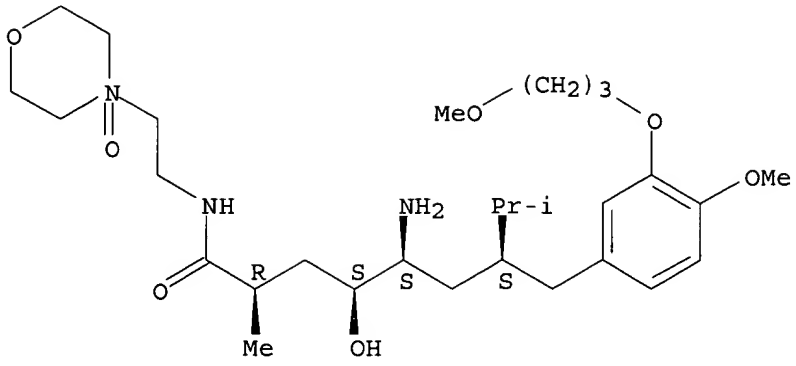
Absolute stereochemistry.



●2 HCl

RN 173334-73-1 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.-methyl-.zeta.-(1-methylethyl)-N-[2-(4-oxido-4-morpholinyl)ethyl]-, monohydrochloride, [.alpha.R-(.alpha.R*,.gamma.S*,.delta.S*,.zeta.S*)]- (9CI) (CA INDEX NAME)

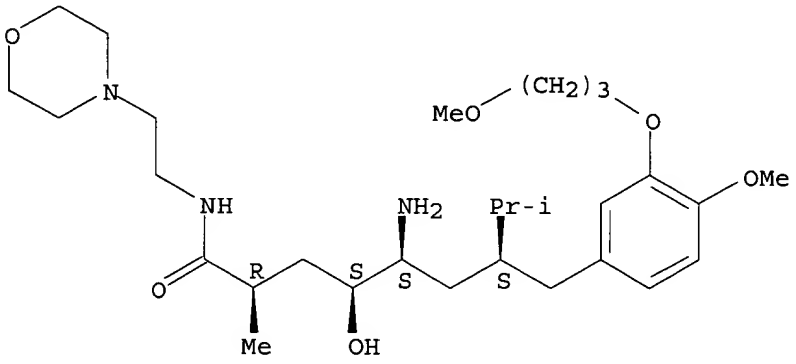
Absolute stereochemistry.



● HCl

RN 173334-85-5 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.-methyl-.zeta.-(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, dihydrochloride, [.alpha.R-(.alpha.R*,.gamma.S*,.delta.S*,.zeta.S*)]- (9CI) (CA INDEX NAME)

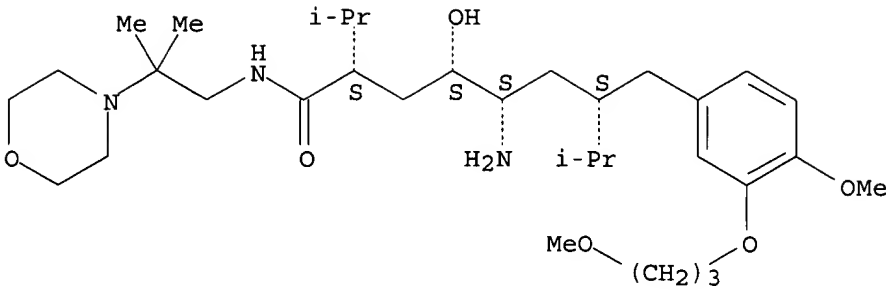
Absolute stereochemistry.



●2 HCl

RN 173335-00-7 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-methyl-2-(4-morpholinyl)propyl]-, dihydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

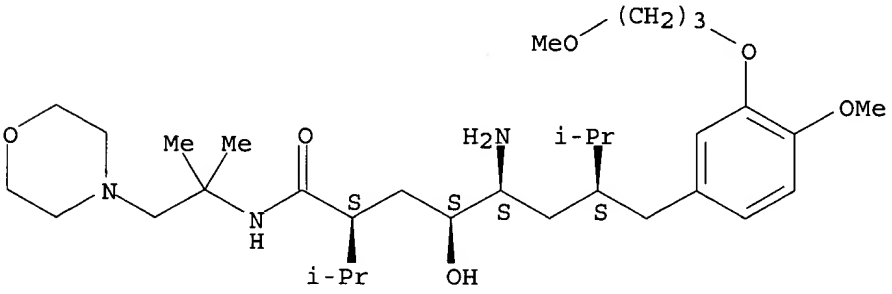
Absolute stereochemistry.



●2 HCl

RN 173335-02-9 CAPLUS
CN Benzeneoctanamide, .delta.-amino-N-[1,1-dimethyl-2-(4-morpholinyl)ethyl]-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-, dihydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

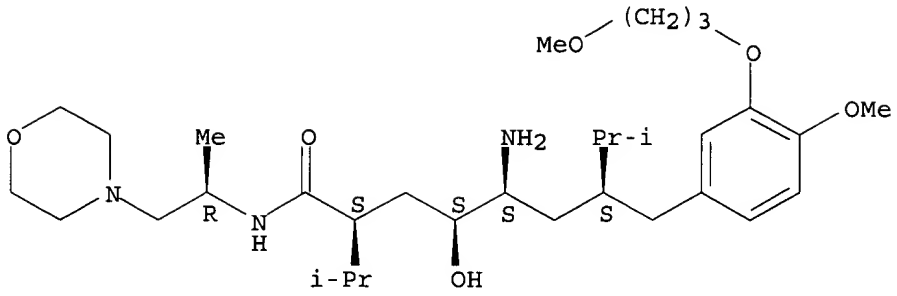
Absolute stereochemistry.



●2 HCl

RN 173335-03-0 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[1-methyl-2-(4-morpholinyl)ethyl]-, dihydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

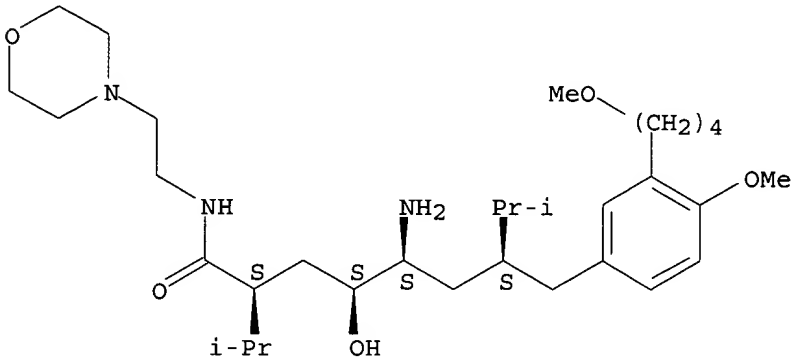
Absolute stereochemistry.



●2 HCl

RN 173335-48-3 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(4-methoxybutyl)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, dihydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]-(9CI) (CA INDEX NAME)

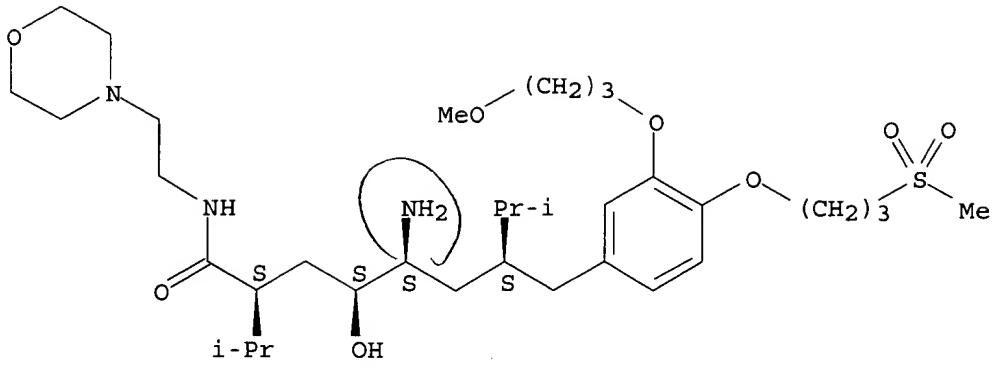
Absolute stereochemistry.



●2 HCl

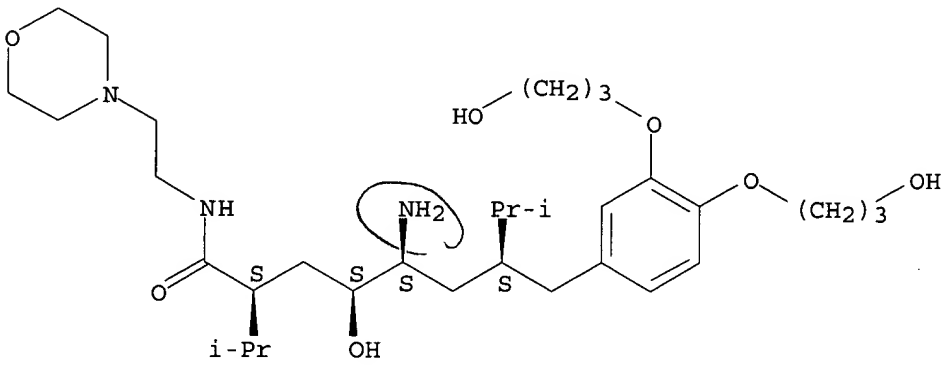
RN 173335-58-5 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-4-[3-(methylsulfonyl)propoxy]-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



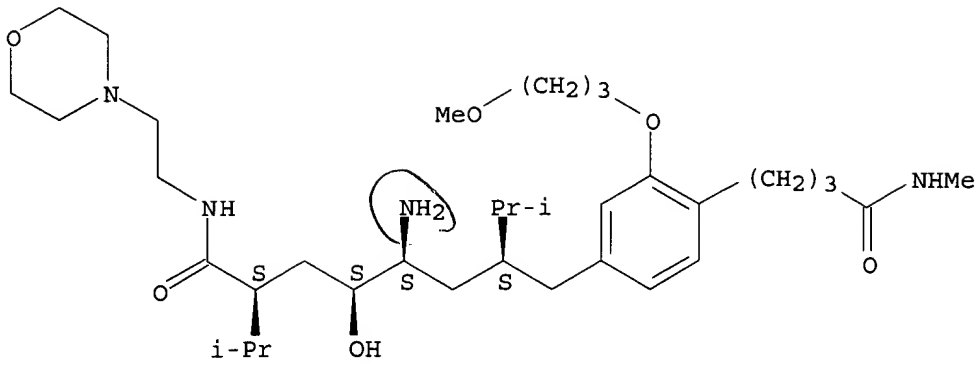
RN 173335-60-9 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-3,4-bis(3-hydroxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



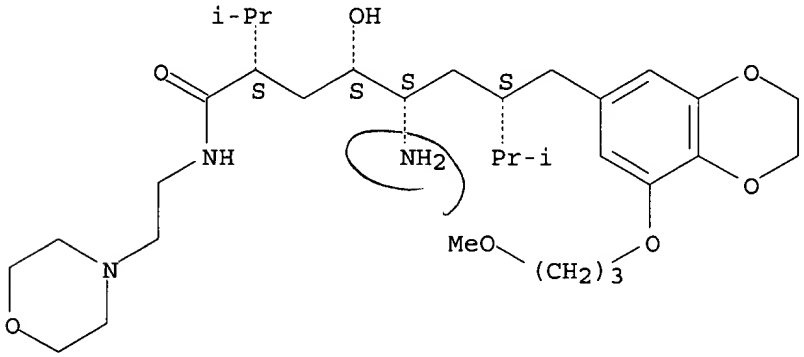
RN 173335-62-1 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-3-(3-methoxypropoxy)-4-[4-(methylamino)-4-oxobutyl]-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



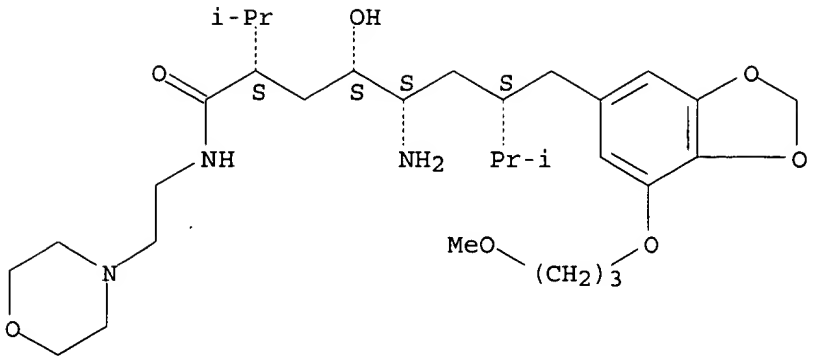
RN 173335-64-3 CAPLUS
CN 1,4-Benzodioxin-6-octanamide, .delta.-amino-2,3-dihydro-.gamma.-hydroxy-8-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



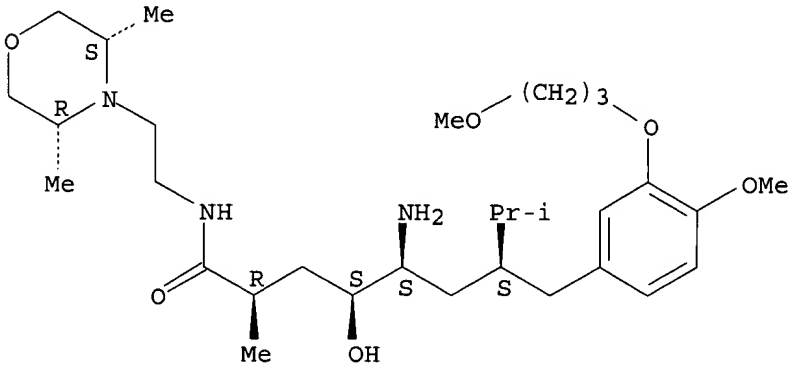
RN 173335-66-5 CAPLUS
CN 1,3-Benzodioxole-5-octanamide, .delta.-amino-.gamma.-hydroxy-7-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 173399-02-5 CAPLUS
CN Benzeneoctanamide, .delta.-amino-N-[2-(3,5-dimethyl-4-morpholinyl)ethyl]-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.-methyl-.zeta.-(1-methylethyl)-, dihydrochloride, [4(.alpha.R)-[3.alpha.,4(.alpha.R*,.gamma.S*,.delta.S*,.zeta.S*),5.alpha.]]- (9CI) (CA INDEX NAME)

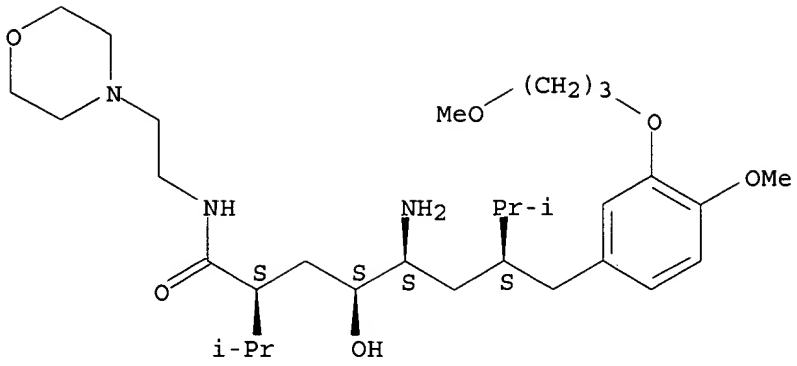
Absolute stereochemistry.



● 2 HCl

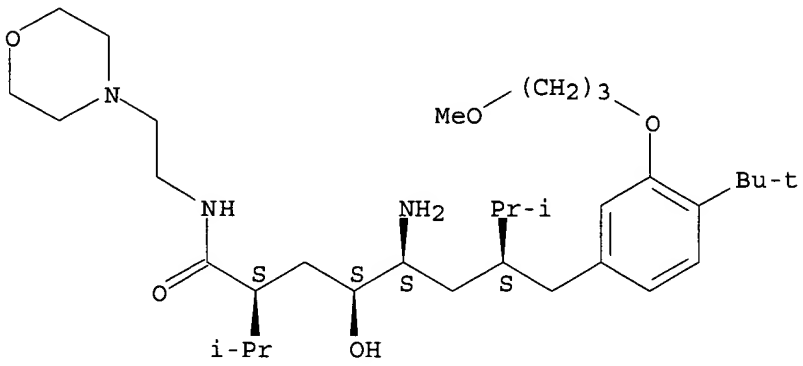
RN 173399-13-8 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



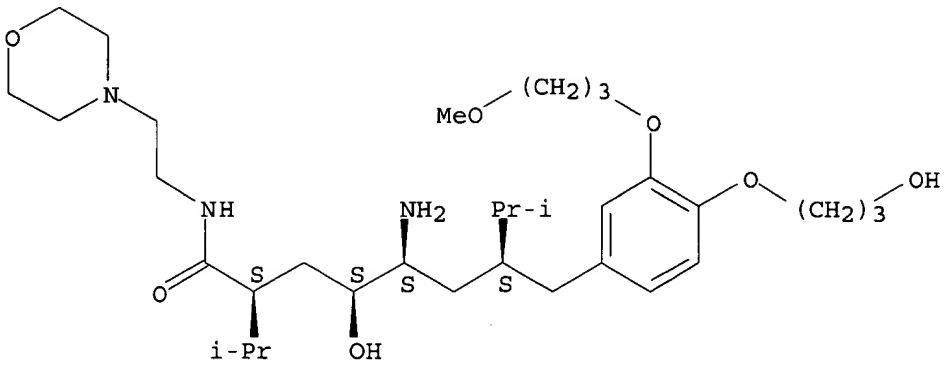
RN 173399-24-1 CAPLUS
CN Benzeneoctanamide, .delta.-amino-4-(1,1-dimethylethyl)-.gamma.-hydroxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



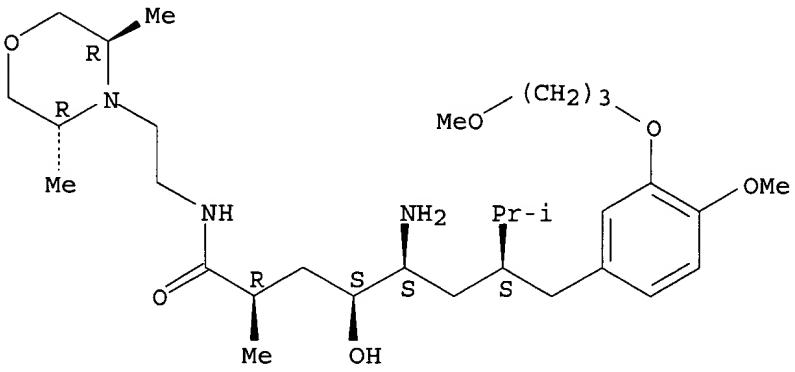
RN 173399-85-4 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-(3-hydroxypropoxy)-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



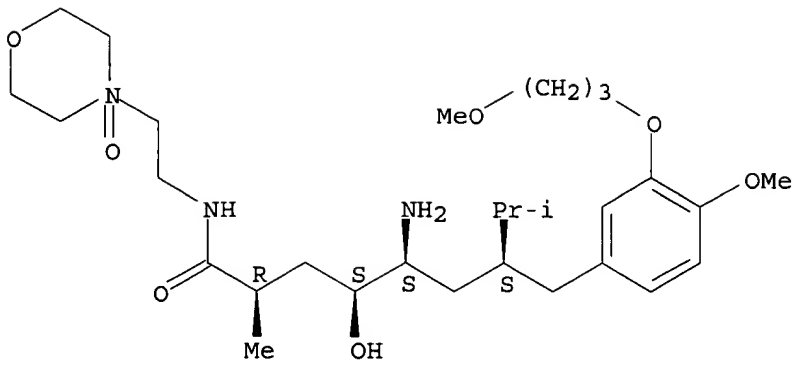
RN 173399-86-5 CAPLUS
CN Benzeneoctanamide, .delta.-amino-N-[2-(3,5-dimethyl-4-morpholinyl)ethyl]-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.-methyl-.zeta.-(1-methylethyl)-, [3R-[3.alpha.,4(.alpha.R*,.gamma.S*,.delta.S*,.zeta.S*),5.beta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



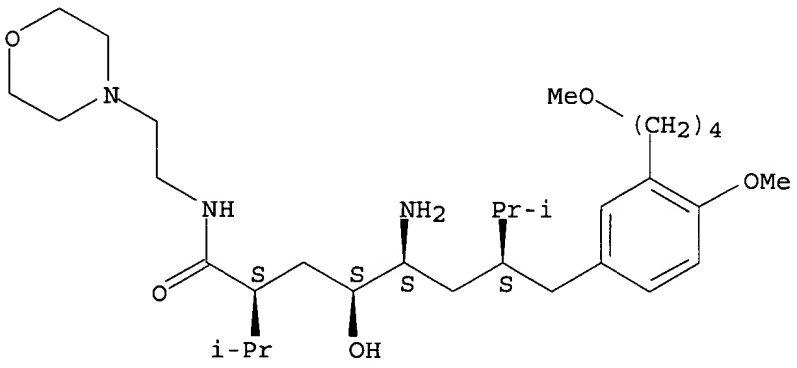
RN 173399-96-7 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.-methyl-.zeta.-(1-methylethyl)-N-[2-(4-oxido-4-morpholinyl)ethyl]-, [.alpha.R-(.alpha.R*,.gamma.S*,.delta.S*,.zeta.S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



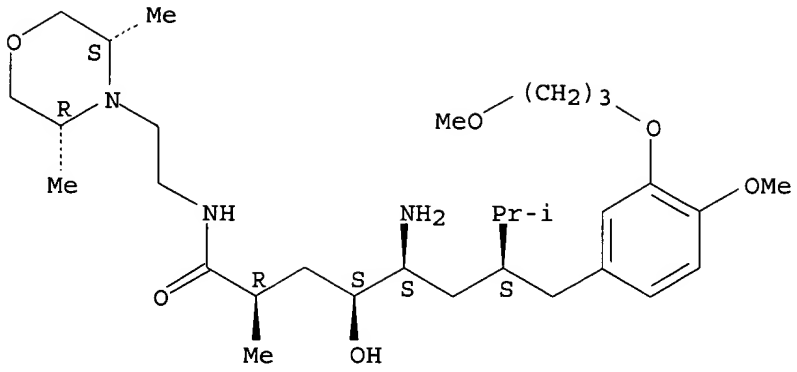
RN 173400-32-3 CAPLUS
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(4-methoxybutyl)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 173521-34-1 CAPLUS
CN Benzeneoctanamide, .delta.-amino-N-[2-(3,5-dimethyl-4-morpholinyl)ethyl]-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.-methyl-.zeta.-(1-methylethyl)-, [4(.alpha.R)-[3.alpha.,4(.alpha.R*,.gamma.S*,.delta.S*,.zeta.R*),5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

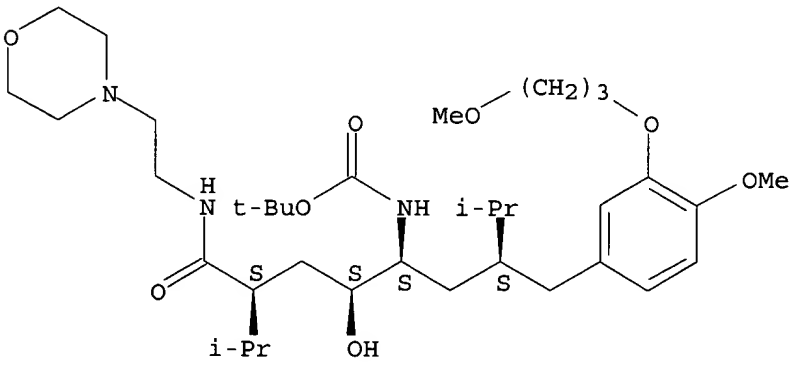


IT **172900-86-6P 173154-14-8P 173336-24-8P**
173336-72-6P 173337-64-9P 173337-65-0P
173337-75-2P 173337-82-1P 173337-93-4P
173337-95-6P 173337-96-7P 173400-59-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .delta.-amino-.gamma.-hydroxy-.omega.-arylalkanoic acid amides as renin inhibitors)

RN 172900-86-6 CAPLUS

CN Carbamic acid, [2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

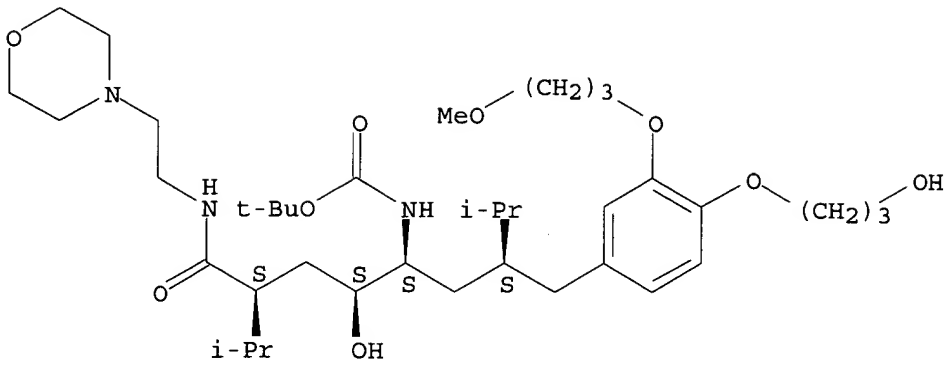
Absolute stereochemistry.



RN 173154-14-8 CAPLUS

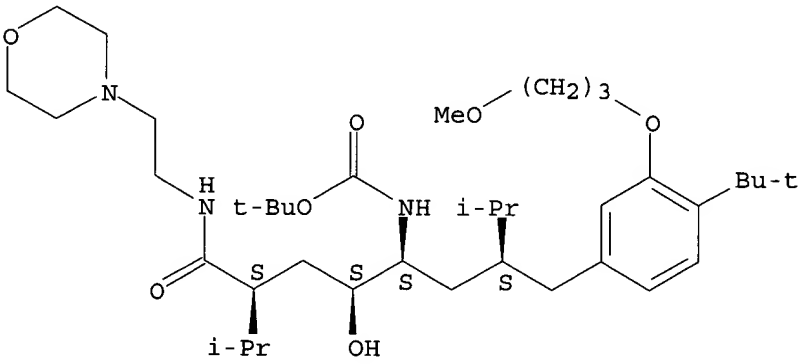
CN Carbamic acid, [2-hydroxy-1-[2-[[4-(3-hydroxypropoxy)-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



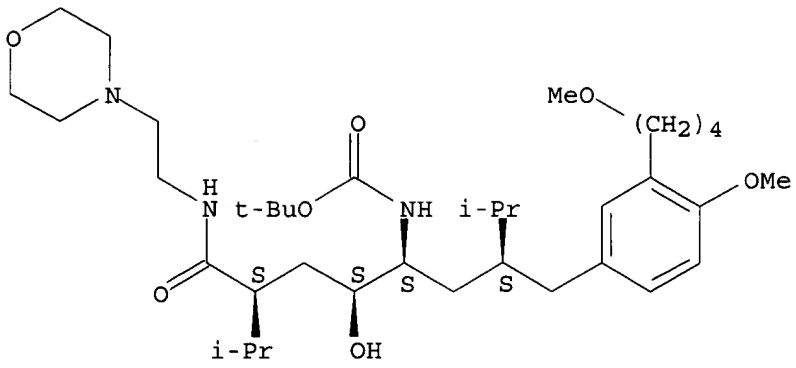
RN 173336-24-8 CAPLUS
CN Carbamic acid, [1-[2-[[4-(1,1-dimethylethyl)-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



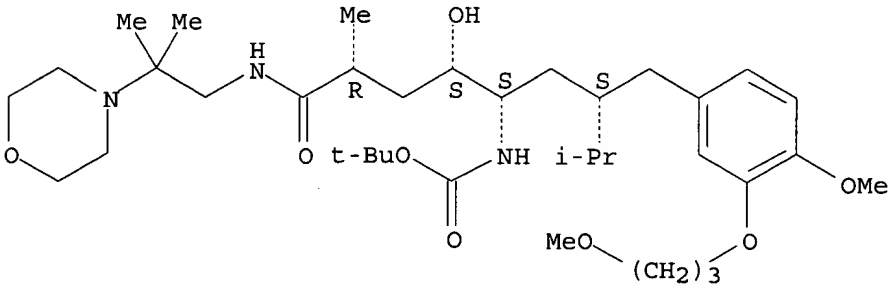
RN 173336-72-6 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[4-methoxy-3-(4-methoxybutyl)phenyl]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



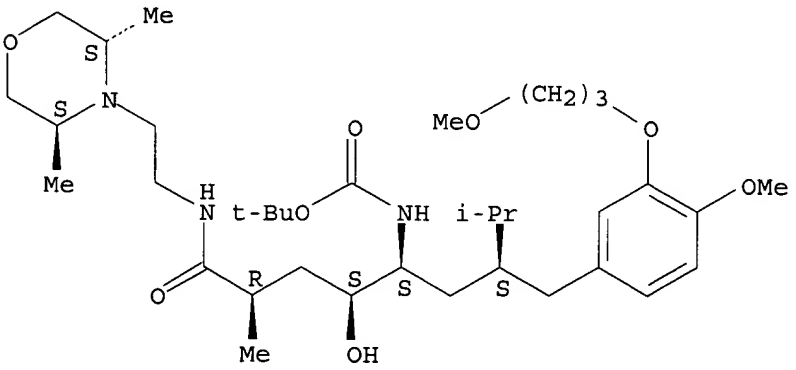
RN 173337-64-9 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-4-methyl-5-[[2-methyl-2-(4-morpholinyl)propyl]amino]-5-oxopentyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 173337-65-0 CAPLUS
CN Carbamic acid, [5-[[2-(3,5-dimethyl-4-morpholinyl)ethyl]amino]-2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-4-methyl-5-oxopentyl]-, 1,1-dimethylethyl ester, [3S-[3.alpha.,4[1R*(R*),2R*,4S*],5.beta.]]- (9CI) (CA INDEX NAME)

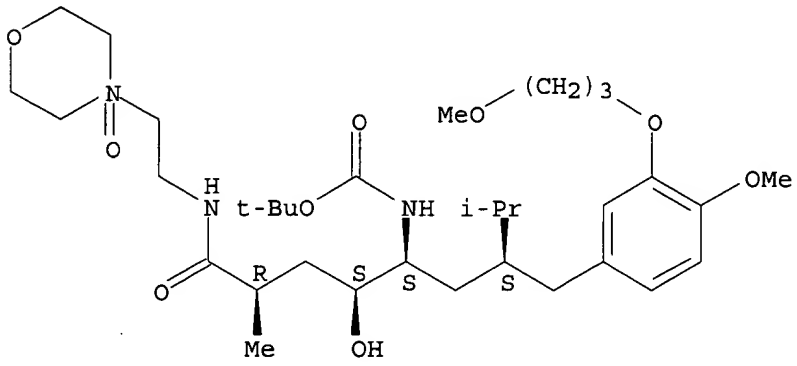
Absolute stereochemistry.



RN 173337-75-2 CAPLUS

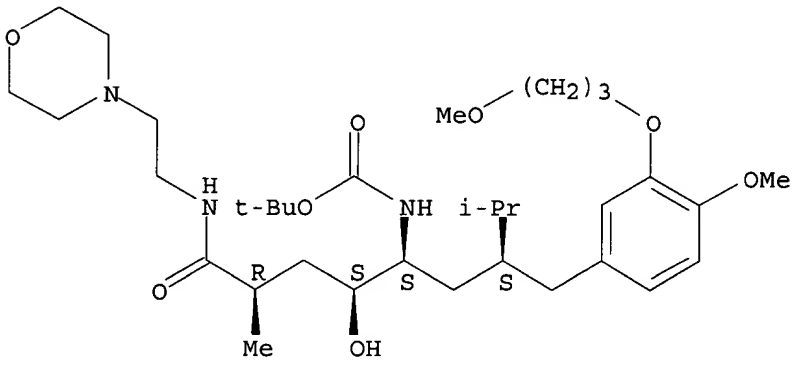
CN Carbamic acid, [2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-4-methyl-5-[[2-(4-oxido-4-morpholinyl)ethyl]amino]-5-oxopentyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



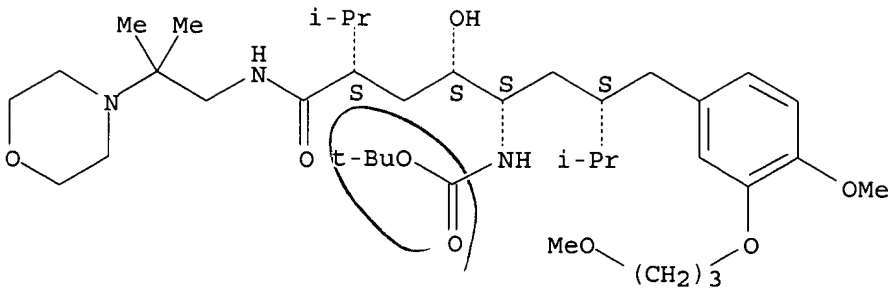
RN 173337-82-1 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-4-methyl-5-[[2-(4-morpholinyl)ethyl]amino]-5-oxopentyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



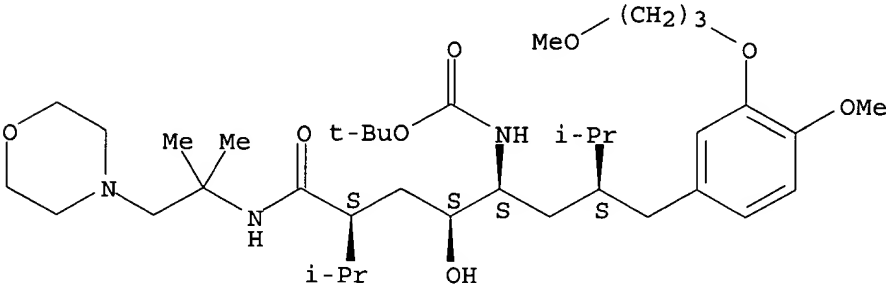
RN 173337-93-4 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-5-methyl-4-[[[2-methyl-2-(4-morpholinyl)propyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



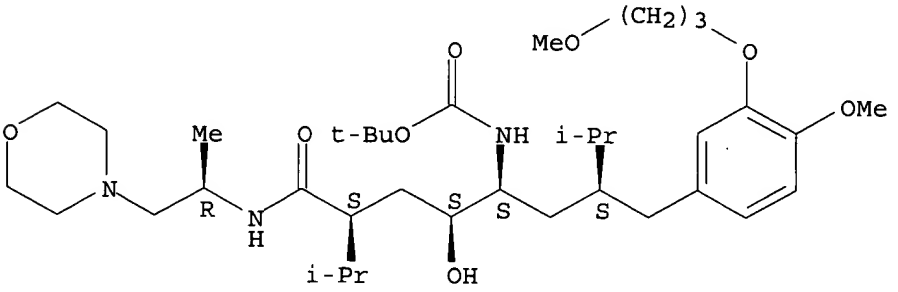
RN 173337-95-6 CAPLUS
CN Carbamic acid, [4-[[[1,1-dimethyl-2-(4-morpholinyl)ethyl]amino]carbonyl]-2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-5-methylhexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



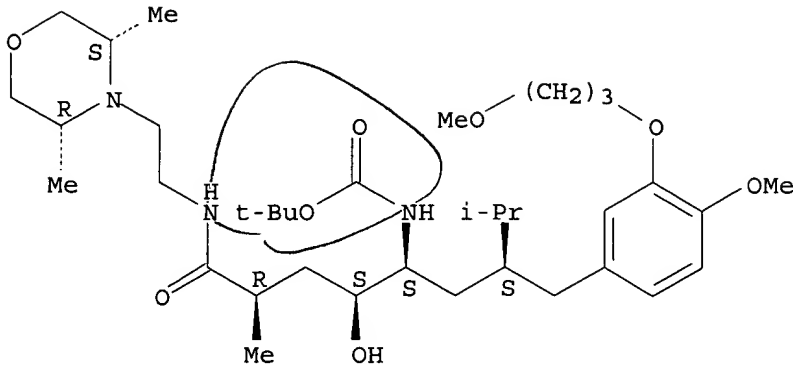
RN 173337-96-7 CAPLUS
CN Carbamic acid, [2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-5-methyl-4-[[[1-methyl-2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*(S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



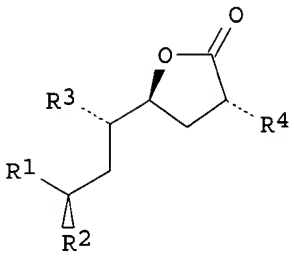
RN 173400-59-4 CAPLUS
CN Carbamic acid, [5-[[2-(3,5-dimethyl-4-morpholinyl)ethyl]amino]-2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-4-methyl-5-oxopentyl]-, 1,1-dimethylethyl ester, [4(1S)-[3.alpha.,4[1R*,1(R*),2R*,4S*],5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


Me
S
O
R
N
Me
H
N
t-BuO
O
NH
i-Pr
MeO
(CH2)3
O
OMe
O
R
S
S
S
Me
OH

L7 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

GI



I

AB Title compds. [I; R1 = (esterified) CO2H, CH2OH, CHO; R2,R4 = (cyclo)aliph, group, (hetero)arylaliph. group, etc.; R3 = N3, (aryl)aliph. group-substituted NH2, protected NH2] were prepd. as intermediates for antihypertensive amides. Thus, 1,4-dibromo-2-butene was dialkylated by 4(S)-benzyl-3-isovealeryloxazolidin-2-one and the brominated product treated with Bu4NN3 to give 3-[2(S)-[2(S)-azido-2(S)-[4(S)-isopropyl-5-oxotetrahydrofuran-2(S)-yl]ethyl]-3-methylbutyryl]-4(S)-benzyloxazolidin-2-one which was treated with H2O2/LiOH to give 2(S)-[2(S)-azido-2(S)-[4(S)-isopropyl-5-oxotetrahydrofuran-2(S)-yl]ethyl]-3-methylbutyric acid.

ACCESSION NUMBER: 1995:995369 CAPLUS
DOCUMENT NUMBER: 124:145882
TITLE: Preparation of chiral 4-(oxotetrahydrofuryl)butyrates and analogs as antihypertensive intermediates
INVENTOR(S): Goeschke, Richard; Herold, Peter; Rigollier, Pascal; Maibaum, Juergen Klaus
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 678514	A1	19951025	EP 1995-810237	19950407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5606078	A	19970225	US 1995-416237	19950404
FI 9501772	A	19951019	FI 1995-1772	19950412
NO 9501442	A	19951019	NO 1995-1442	19950412
AU 9516420	A1	19951026	AU 1995-16420	19950412
CA 2147052	AA	19951019	CA 1995-2147052	19950413
HU 72110	A2	19960328	HU 1995-1077	19950414
JP 08053434	A2	19960227	JP 1995-92526	19950418
US 5654445	A	19970805	US 1996-674555	19960702
US 5627182	A	19970506	US 1996-687878	19960725
US 5646143	A	19970708	US 1996-687277	19960725
US 5705658	A	19980106	US 1997-800671	19970214

PRIORITY APPLN. INFO.:
CH 1994-1169 A 19940418
CH 1995-246 A 19950130
US 1995-416242 A3 19950404
US 1996-687277 A3 19960725

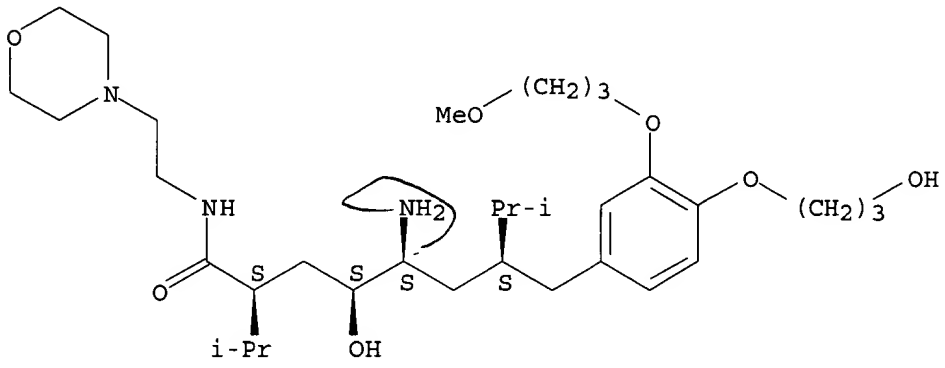
OTHER SOURCE(S): MARPAT 124:145882

IT **173154-15-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of chiral 4-(oxotetrahydrofuryl)butyrates and analogs as antihypertensive intermediates)

RN 173154-15-9 CAPLUS

CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-(3-hydroxypropoxy)-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, monohydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



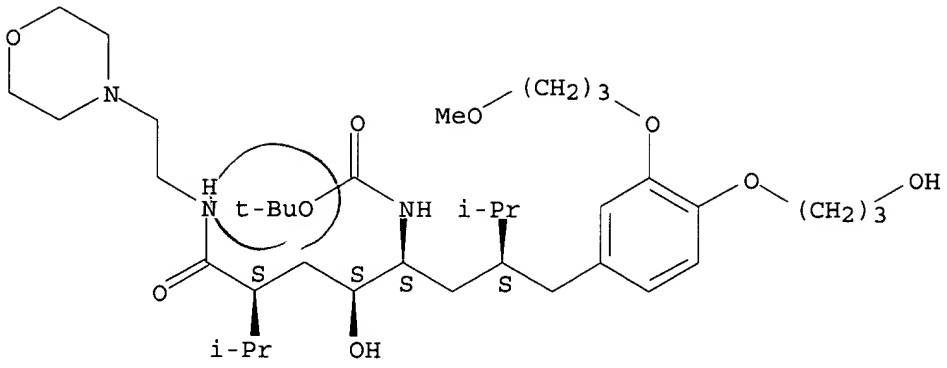
● HCl

IT **173154-14-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of chiral 4-(oxotetrahydrofuryl)butyrates and analogs as antihypertensive intermediates)

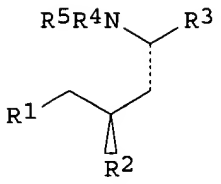
RN 173154-14-8 CAPLUS

CN Carbamic acid, [2-hydroxy-1-[2-[[4-(3-hydroxypropoxy)-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


O
N
H
N
t-BuO
O
NH
i-Pr
MeO
(CH2)3
O
O
(CH2)3
OH
O
S
S
S
S
i-Pr
OH

L7 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I

AB Title compds. [I; R1 = aliphatyl, cycloaliphatyl, aryl, heteroaryl, protected or etherified OH, etherified SH, etc.; R2 = aliphatyl, cycloaliphatyl, araliphatyl, heteroaraliphatyl, etc.; R1r2 = divalent aliphatyl; R3 = (esterified) carboxy, formyl, hydroxymethyl; R4 = H, aliphatyl, araliphatyl, protecting group; R5 = H, aliphatyl], were prepd. Thus, glycine anhydride was stirred 64 h with Et3OBF4 in CH2Cl2 to give 76% 3,6-diethoxy-2,5-dihydropyrazine. The latter in THF at -40.degree. was treated with BuLi and then with 2(R)-[4-methoxy-3-(3-methoxypropoxy)benzyl]-3-methylbutyl bromide; the mixt. was stirred 18 h at -20.degree. to give 2(S)-[2(S)-[4-methoxy-3-(3-methoxypropoxy)benzyl]-3-methylbutyl]-3,6-diethoxy-2,5-dihydropyran. This was stirred 30 min. with HCl in MeCN to give Et 2(S)-amino-4(S)-[4-methoxy-3-(3-methoxypropoxy)benzyl]-5-methylhexanoate.

ACCESSION NUMBER: 1995:995203 CAPLUS
DOCUMENT NUMBER: 124:117982
TITLE: Preparation of .alpha.-amino alkanoic acids and reduction products as intermediates in the preparation of renin inhibitors.
INVENTOR(S): Goeschke, Richard
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 678500	A1	19951025	EP 1995-810238	19950407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5659065	A	19970819	US 1995-416240	19950404
FI 9501773	A	19951019	FI 1995-1773	19950412
NO 9501443	A	19951019	NO 1995-1443	19950412
AU 9516423	A1	19951026	AU 1995-16423	19950412
CA 2147044	AA	19951019	CA 1995-2147044	19950413
JP 08027079	A2	19960130	JP 1995-92827	19950418
US 5654445	A	19970805	US 1996-674555	19960702
US 5627182	A	19970506	US 1996-687878	19960725
US 5646143	A	19970708	US 1996-687277	19960725
US 5705658	A	19980106	US 1997-800671	19970214

PRIORITY APPLN. INFO.:
CH 1994-1169 A 19940418
CH 1995-247 A 19950130
US 1995-416242 A3 19950404
US 1996-687277 A3 19960725

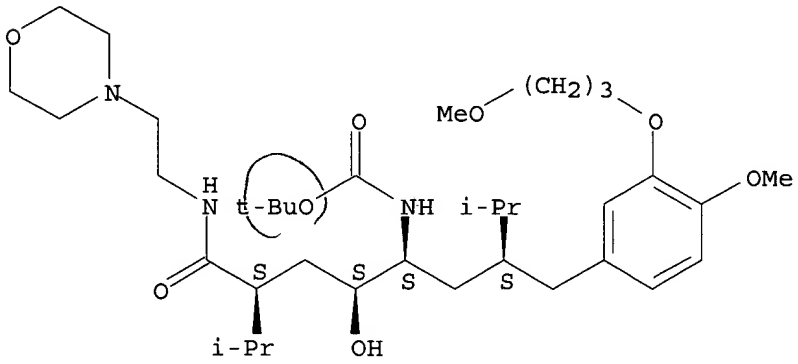
OTHER SOURCE(S): MARPAT 124:117982

IT **172900-86-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .alpha.-amino alkanoic acids and redn. products as intermediates in the prepn. of renin inhibitors)

RN 172900-86-6 CAPLUS

CN Carbamic acid, [2-hydroxy-1-[2-[[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl]-3-methylbutyl]-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

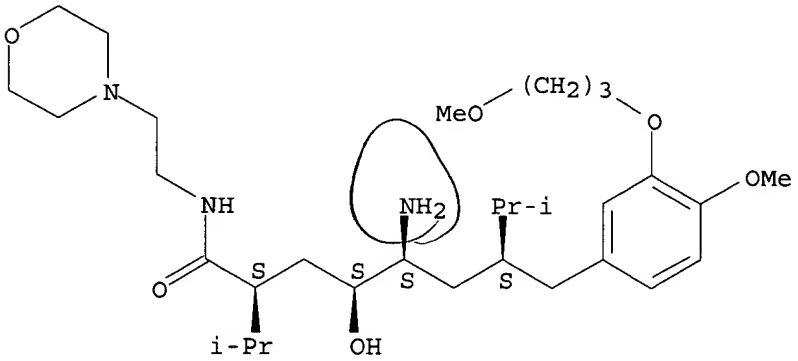


IT **172900-85-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of .alpha.-amino alkanoic acids and redn. products as intermediates in the prepn. of renin inhibitors)

RN 172900-85-5 CAPLUS

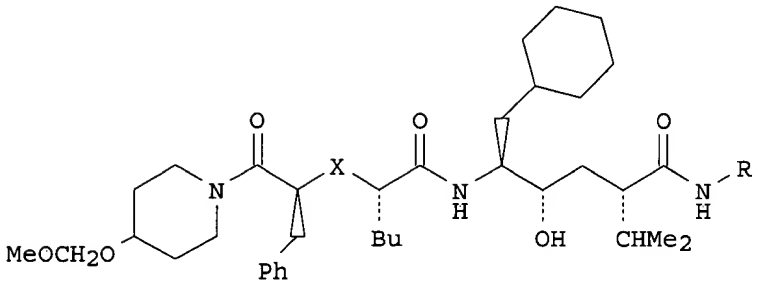
CN Benzeneoctanamide, .delta.-amino-.gamma.-hydroxy-4-methoxy-3-(3-methoxypropoxy)-.alpha.,.zeta.-bis(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, dihydrochloride, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*,.zeta.R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L7 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I

AB The aim of this study was the discovery of nonpeptide renin inhibitors with much improved oral absorption, bioavailability, and efficacy, for use as antihypertensive agents. Prior efforts led to the identification of A-74273 [I; X = O, R = 3-(4-morpholino)propyl], with a bioavailability of 26 .+-. 10% [10 mg/kg intraduodenally (id.), dog]. In vivo metab. studies of A-74273 showed that the morpholino moiety underwent metabolic degrdn. Computer modeling of A-74273 bound to renin indicated that the C-terminus was involved in a hydrogen-bonding network. New C-terminal groups were examd. in two series of nonpeptides for effects on renin binding potency, lipophilicity (log P), and aq. soly. Those groups which possessed multiple hydrogen-bonding ability (3,5-diaminotriazole, cyanoguanidines, morpholino) provided particularly potent renin binding. Intraduodenal bioavailabilities of selected compds., evaluated in rats, ferrets, and dogs, were higher for inhibitors with moderate soly. as well as moderate lipophilicity, in general. Although the abs. values varied substantially among species, the relative ordering of the inhibitors in terms of absorption and bioavailability was reasonably consistent. Such well absorbed inhibitors, e.g. I [X = NH, R = 3-(4-morpholino)propyl, 2-(4-morpholino)ethyl, 2-methyl-2-(4-morpholino)propyl], were demonstrated as highly efficacious hypotensive agents in the salt-depleted dog. The discovery of a series of efficacious nonpeptide renin inhibitors based on the 3-azaglutaramide P2-P4 replacement are reported, the best of which showed id. bioavailabilities >50% in dog.

ACCESSION NUMBER: 1995:43414 CAPLUS
DOCUMENT NUMBER: 122:161289
TITLE: Nonpeptide Renin Inhibitors with Good Intraduodenal Bioavailability and Efficacy in Dog
AUTHOR(S): Boyd, Steven A.; Fung, Anthony K. L.; Baker, William R.; Mantei, Robert A.; Stein, Herman H.; Cohen, Jerome; Barlow, Jennifer L.; Klinghofer, Vered; Wessale, Jerry L.; et al.
CORPORATE SOURCE: Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL, 60064, USA
SOURCE: Journal of Medicinal Chemistry (1994), 37(19), 2991-3007
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **142708-09-6P 142708-24-5P 142708-26-7P 161316-26-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

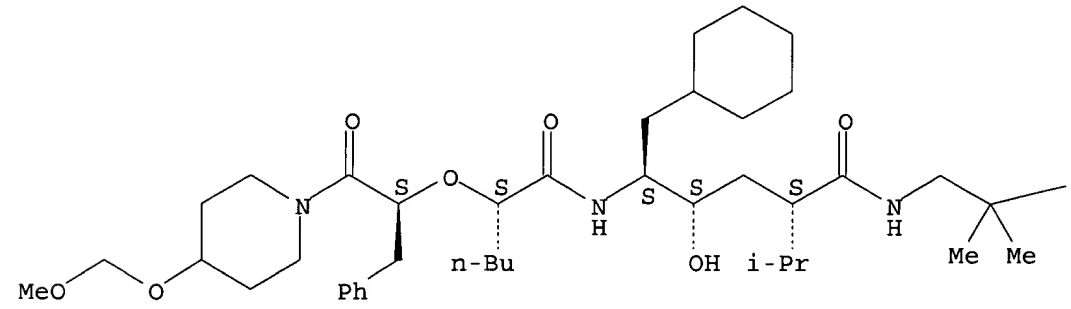
(prepn., bioavailability, and renin inhibitory activity of nonpeptide renin inhibitors with good intraduodenal bioavailability and efficacy in dog)

RN 142708-09-6 CAPLUS

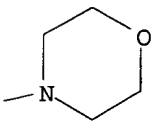
CN Cyclohexanehexanamide, .gamma.-hydroxy-.delta.-[[2-[2-[4-(methoxymethoxy)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethoxy]-1-oxohexyl]amino]-.alpha.-(1-methylethyl)-N-[2-methyl-2-(4-morpholinyl)propyl]-, [.alpha.S-[.alpha.R*,.gamma.R*,.delta.R*[R*(R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



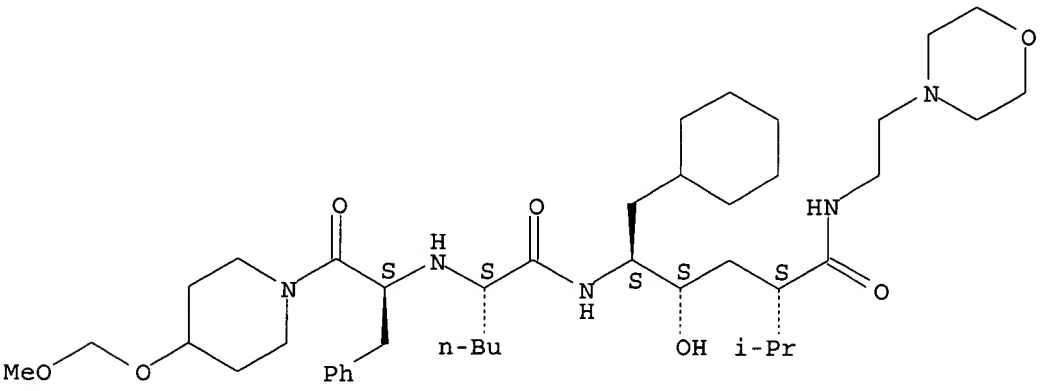
PAGE 1-B



RN 142708-24-5 CAPLUS

CN Cyclohexanehexanamide, .gamma.-hydroxy-.delta.-[[2-[[2-[4-(methoxymethoxy)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethyl]amino]-1-oxohexyl]amino]-.alpha.-(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-[.alpha.R*,.gamma.R*,.delta.R*[R*(R*)]]]- (9CI) (CA INDEX NAME)

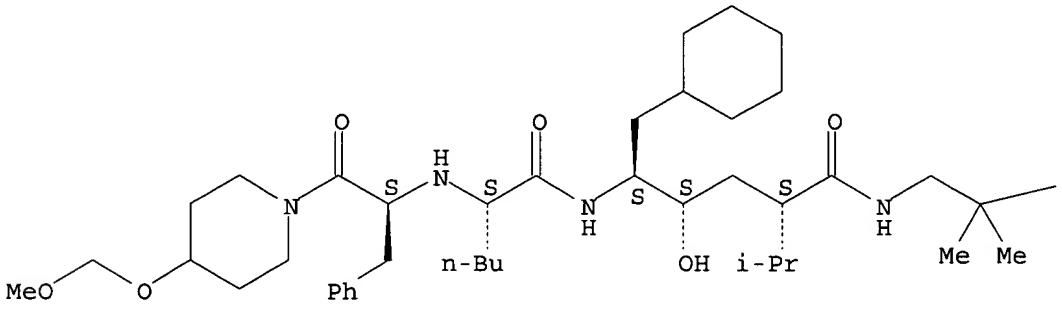
Absolute stereochemistry.



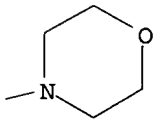
RN 142708-26-7 CAPLUS
CN Cyclohexanehexanamide, .gamma.-hydroxy-.delta.-[[2-[[2-[4-(methoxymethoxy)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethyl]amino]-1-oxohexyl]amino]-.alpha.-(1-methylethyl)-N-[2-methyl-2-(4-morpholinyl)propyl]-, [.alpha.S-[.alpha.R*,.gamma.R*,.delta.R*[R*(R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

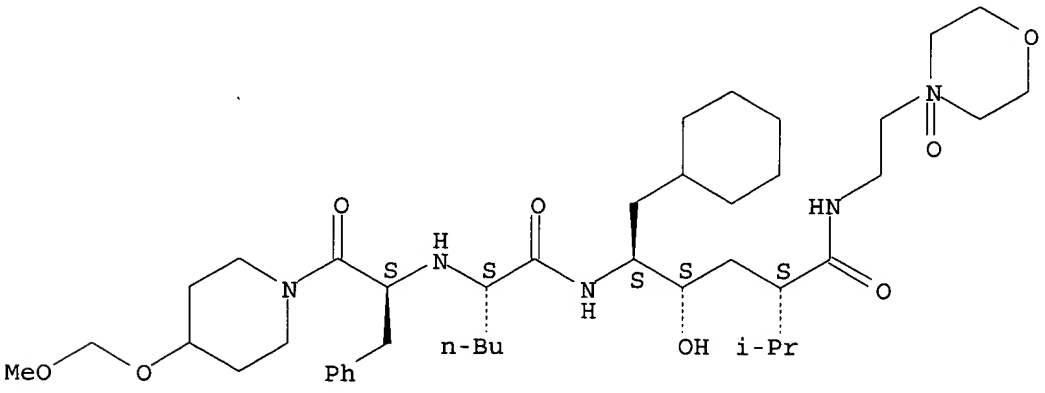


PAGE 1-B



RN 161316-26-3 CAPLUS
CN Cyclohexanehexanamide, .gamma.-hydroxy-.delta.-[[2-[[2-[4-(methoxymethoxy)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethyl]amino]-1-oxohexyl]amino]-.alpha.-(1-methylethyl)-N-[2-(4-oxido-4-morpholinyl)ethyl]-, [.alpha.S-[.alpha.R*,.gamma.R*,.delta.R*[R*(R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

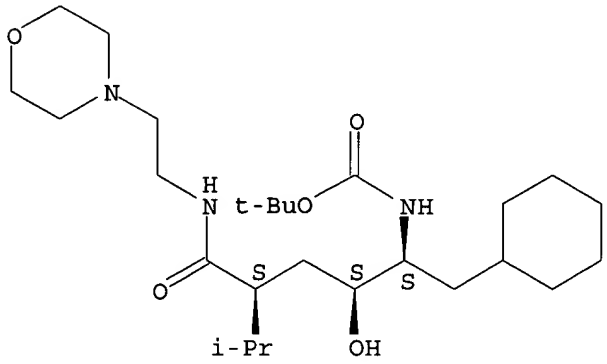


IT **142688-87-7P 142688-89-9P 161316-20-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., bioavailability, and renin inhibitory activity of nonpeptide renin inhibitors with good intraduodenal bioavailability and efficacy in dog)

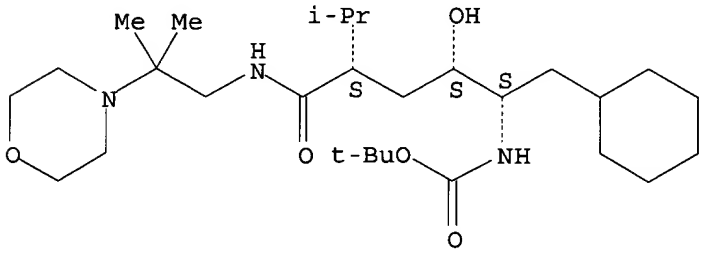
RN 142688-87-7 CAPLUS
CN Carbamic acid, [1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



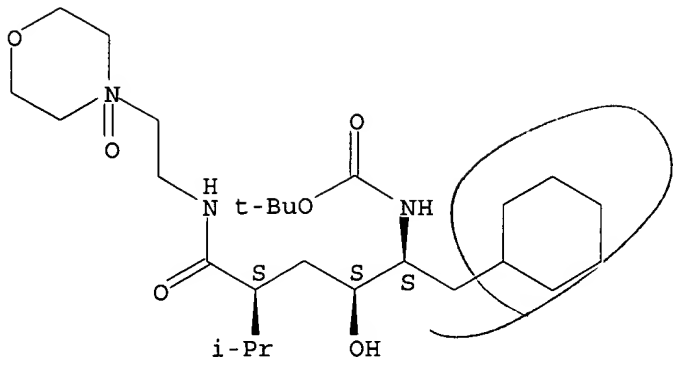
RN 142688-89-9 CAPLUS
CN Carbamic acid, [1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-methyl-2-(4-morpholinyl)propyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

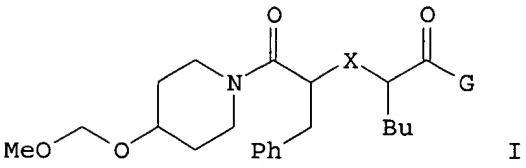


RN 161316-20-7 CAPLUS
CN Carbamic acid, [1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-oxido-4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


O
N
O
H
N
t-BuO
O
NH
O
S
S
S
i-Pr
OH

L7 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I

AB Title compds. I (X = O, NH, S; G = mimic of the Leu-Val cleavage site of angiotensinogen; with one specifically excluded compd.) and their salts, esters, and prodrugs, are prepd. for treatment of a variety of conditions, esp. hypertension and congestive heart failure. For example, amidation of 2(S)-[[3-(tert-butoxycarbonyl)-2,2-dimethyl-4(S)-cyclohexylmethyl-5(S)-oxazolidinyl]methyl]-3-methylbutanoic acid with H2N(CH2)3NHCO2CH2Ph, followed by deprotection with CF3CO2H, hydrolysis, peptide coupling with 2(S)-[1(S)-[4-(methoxymethoxy)piperidin-1-ylcarbonyl]-2-phenylethoxy]hexanoic acid, hydrogenolytic deprotection, and acetylation, gave (S,S)-I [X = O; G = (S,S,S)-NHCH(CH2R)CH(OH)CH2CH(CHMe2)CONH(CH2)3NHAc; R = cyclohexyl] (II). The IC50 of II for inhibiting the conversion of angiotensinogen to angiotensin I by human renal renin was 1.0 nM.

ACCESSION NUMBER: 1992:490802 CAPLUS
DOCUMENT NUMBER: 117:90802
TITLE: Preparation of [[[(methoxymethoxy)piperidinyl]carbonyl](phenyl)ethoxy]hexanamide and -ethyl]norleucinamide derivatives as renin inhibitors
INVENTOR(S): Baker, William R.; Boyd, Steven A.; Fung, Anthony K. L.; Stein, Herman H.; Denissen, Jon F.; Hutchins, Charles W.; Rosenberg, Saul H.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

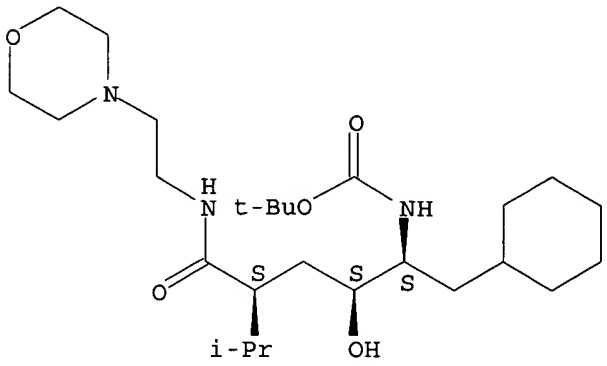
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9203429	A1	19920305	WO 1991-US5524	19910802
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5122514	A	19920616	US 1991-680811	19910409
US 5178877	A	19930112	US 1991-737093	19910729
US 5244910	A	19930914	US 1991-736364	19910731
AU 9185315	A1	19920317	AU 1991-85315	19910802
AU 653959	B2	19941020		
EP 543936	A1	19930602	EP 1991-916458	19910802
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06500111	T2	19940106	JP 1991-515076	19910802
WO 9302667	A1	19930218	WO 1992-US5923	19920715
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9223924	A1	19930302	AU 1992-23924	19920715

US 5389647 A 19950214 US 1993-71747 19930609
PRIORITY APPLN. INFO.: US 1990-568557 19900815
US 1991-680811 19910409
US 1990-513367 19900423
US 1991-632595 19910104
US 1991-678111 19910404
US 1991-683663 19910415
US 1991-737093 19910729
WO 1991-US5524 19910802
WO 1992-US5923 19920715
OTHER SOURCE(S): MARPAT 117:90802

IT **142688-87-7P 142688-89-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for renin inhibitors)

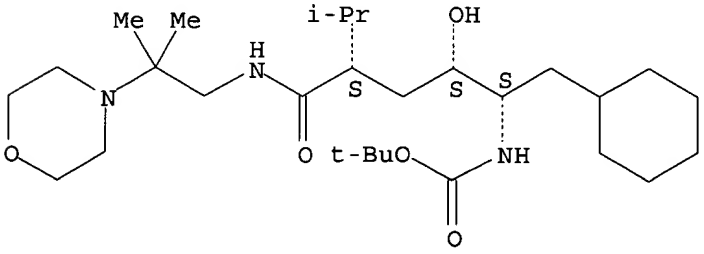
RN 142688-87-7 CAPLUS
CN Carbamic acid, [1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142688-89-9 CAPLUS
CN Carbamic acid, [1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-methyl-2-(4-morpholinyl)propyl]amino]carbonyl]hexyl]-, 1,1-dimethylethyl ester, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



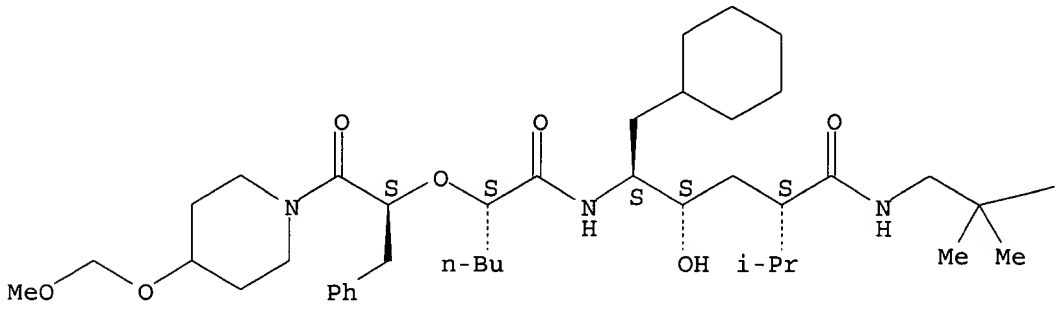
IT **142708-09-6P 142708-24-5P 142708-26-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as renin inhibitor)

RN 142708-09-6 CAPLUS

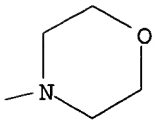
CN Cyclohexanehexanamide, .gamma.-hydroxy-.delta.-[[2-[2-[4-(methoxymethoxy)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethoxy]-1-oxohexyl]amino]-.alpha.-(1-methylethyl)-N-[2-methyl-2-(4-morpholinyl)propyl]-, [.alpha.S-[.alpha.R*,.gamma.R*,.delta.R*[R*(R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



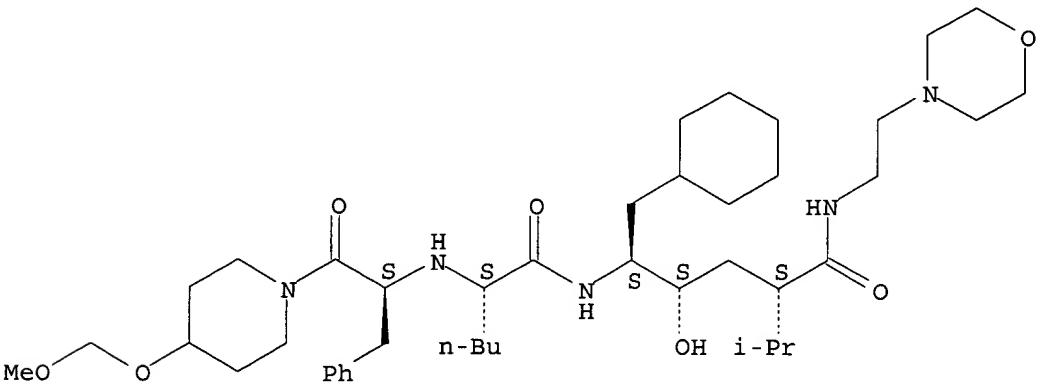
PAGE 1-B



RN 142708-24-5 CAPLUS

CN Cyclohexanehexanamide, .gamma.-hydroxy-.delta.-[[2-[[2-[4-(methoxymethoxy)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethyl]amino]-1-oxohexyl]amino]-.alpha.-(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-[.alpha.R*,.gamma.R*,.delta.R*[R*(R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



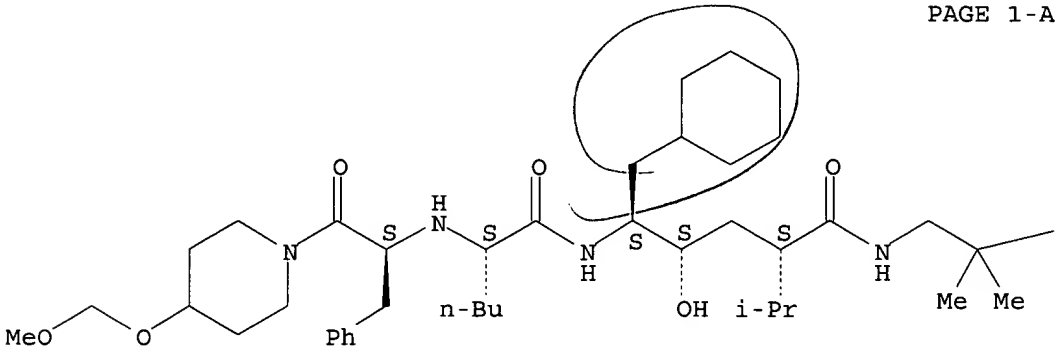
RN 142708-26-7 CAPLUS

CN Cyclohexanehexanamide, .gamma.-hydroxy-.delta.-[[2-[[2-[4-(methoxymethoxy)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethyl]amino]-1-oxohexyl]amino]-

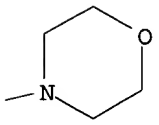
.alpha.-(1-methylethyl)-N-[2-methyl-2-(4-morpholinyl)propyl]-, [.alpha.S-[.alpha.R*,.gamma.R*,.delta.R*[R*(R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

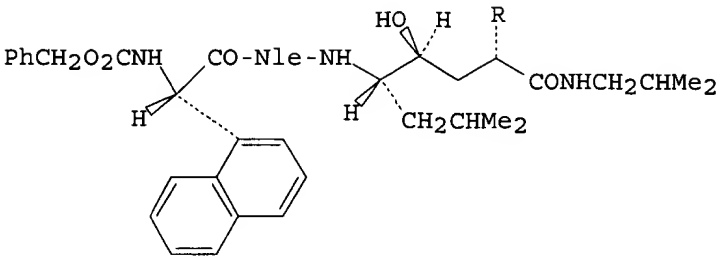


PAGE 1-B



L7 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

GI



I

AB The synthesis and structure-activity relationships of transition-state renin inhibitors, e.g. I [R = H, Me, Et, Pr, CHMe2, CH2CHMe2, Me3CO2CNHCH2, HOCH2CH2, HOCH2CH2CH2, H2NCH2CH2CH2 HOCHMeCH2, HOCH2CH(OH)CH2], contg. the homostatine analogs at the scissile bond are described. These inhibitors incorporate the amino acid side chains corresponding to positions 7-12 (P4-P2') of angiotensinogen. Et, 2-hydroxyethyl, and 3-hydroxypropyl groups at position 2 of the homostatine analogs (P1') are more effective for increasing potency than the iso-Pr group. A combination of residues at P1, P3, and P4 is important for potency and this result suggests that S1, S3, and S4 form a huge hydrophobic core together in renin.

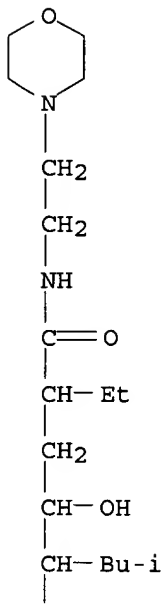
ACCESSION NUMBER: 1992:470294 CAPLUS
DOCUMENT NUMBER: 117:70294
TITLE: Renin inhibitors. I. Synthesis and structure-activity relationships of transition-state inhibitors containing homostatine analogs at the scissile bond
AUTHOR(S): Atsuumi, Shugo; Nakano, Masato; Koike, Yutaka; Tanaka, Seiichi; Matsuyama, Kenji; Nakano, Makiko; Morishima, Hajime
CORPORATE SOURCE: Explor. Res. Lab., Banyu Pharm. Co., Ltd., Tokyo, 153, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1992), 40(2), 364-70
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **141713-96-4 141782-83-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(renin inhibitory activity of)

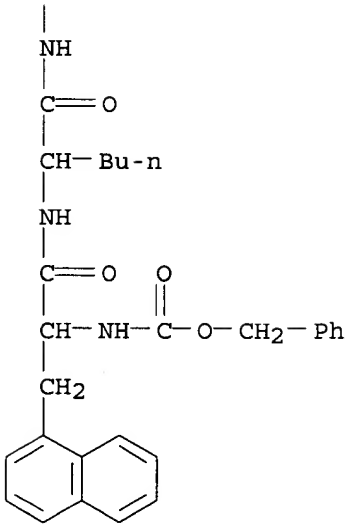
RN 141713-96-4 CAPLUS

CN L-Norleucinamide, 3-(1-naphthalenyl)-N-[(phenylmethoxy)carbonyl]-L-alanyl-N-[2-hydroxy-1-(2-methylpropyl)-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4S*)]- (9CI) (CA INDEX NAME)

PAGE 1-A

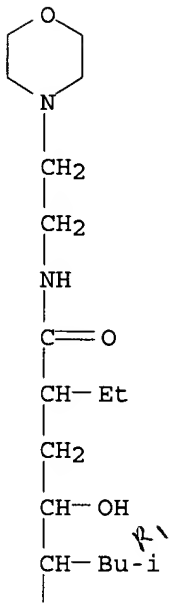


PAGE 2-A

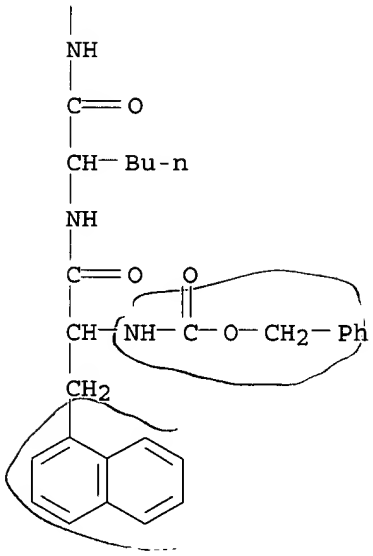


RN 141782-83-4 CAPLUS
CN L-Norleucinamide, 3-(1-naphthalenyl)-N-[(phenylmethoxy)carbonyl]-L-alanyl-N-[2-hydroxy-1-(2-methylpropyl)-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

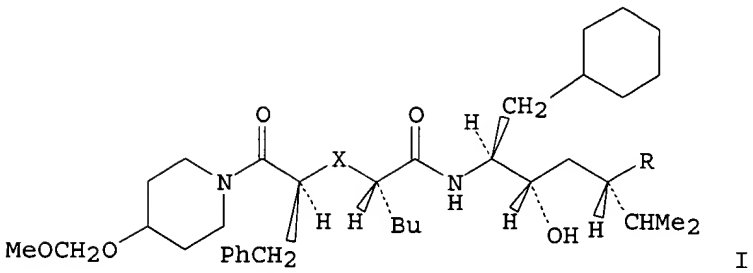
PAGE 1-A



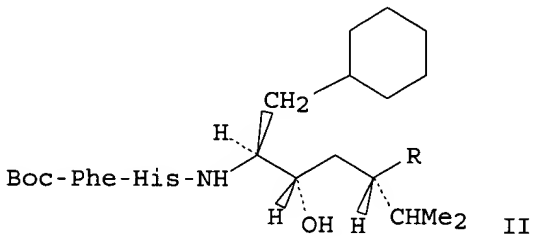
PAGE 2-A



L7 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I



II

AB The development of a series of sol., potent, and bioavailable nonpeptide renin inhibitors, e.g. I (X = O, NH; R = NHCO2CH2CH2R1, CONR2CH2CH2R1, R1 = Me, CHMe2, NMe2, CH2NMe2, pyrrolidino, morpholino, 2-pyridyl, R2 = H, Me) and II (Boc = Me3CO2C, R = NHCO2CH2CH2R1) is described. These inhibitors were derived from a series of novel nonpeptide renin inhibitors recently identified in the author's labs. by alteration of the nature of the C-terminus (P2') of the mols. Introduction of basic substituents into modified hydroxyethylene dipeptide isosteres gave inhibitors with improved soly. as well as improved potency against human plasma renin. In addn., these modifications produced inhibitors which displayed markedly improved intraduodenal bioavailability in both the ferret and cynomolgus monkey. Data is also presented which demonstrate excellent efficacy in the monkey for A-74273 I (X = O, R = CONHCH2CH2CH2R1, R1 = morpholino) with an intraduodenal bioavailability of 16 .+-. 4% in the monkey, compared to 1.7 .+-. 0.5% for the dipeptide renin inhibitor enalkiren (A-64662). A-74273 is an example of a nonpeptide inhibitor which possesses a good balance of the desirable properties of potency, soly., and lipophilicity, and which is well absorbed into the intestine.

ACCESSION NUMBER: 1992:256003 CAPLUS
DOCUMENT NUMBER: 116:256003
TITLE: C-Terminal modifications of nonpeptide renin inhibitors: improved oral bioavailability via modification of physicochemical properties
AUTHOR(S): Boyd, Steven A.; Fung, Anthony K. L.; Baker, William R.; Mantei, Robert A.; Armiger, Yoek Lin; Stein, Herman H.; Cohen, Jerome; Egan, David A.; Barlow, Jennifer L.; et al.
CORPORATE SOURCE: Pharm. Prod. Div., Abbott Lab., Abbott Park, IL, 60064, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(10), 1735-46
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal

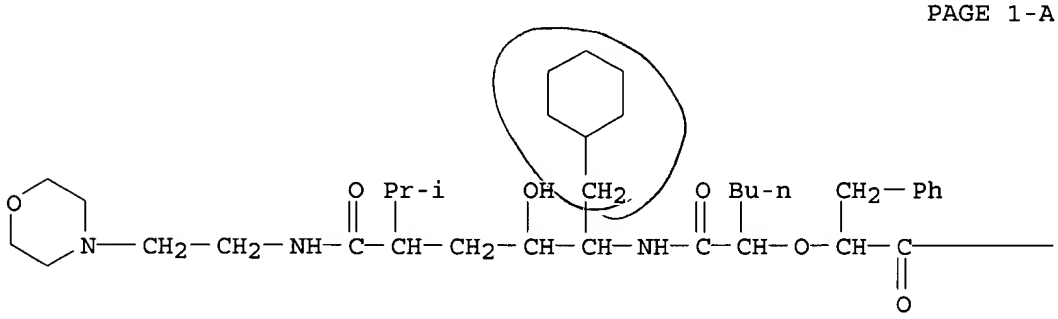
LANGUAGE: English

IT **140660-97-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., partition coeff., and renin inhibitory activity of)

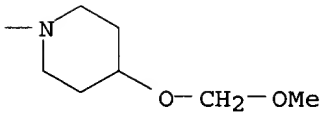
RN 140660-97-5 CAPLUS

CN Cyclohexanehexanamide, .gamma.-hydroxy-.delta.-[[2-[2-[4-(methoxymethoxy)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethoxy]-1-oxohexyl]amino]-.alpha.-(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-[.alpha.R*,.gamma.R*,.delta.R*[R*(R*)]]]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L7 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

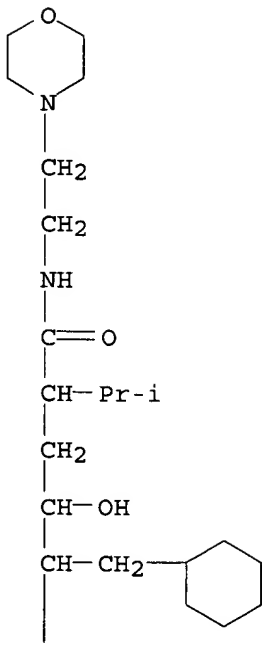
AB Syntheses of precursors I (R = Me2CH, R1= H; R = H, R1 = Me2CH) for renin inhibitors possessing hydroxyethylene isostere residue from 2,4,6-tri-O-acetyl-D-glucal via lactone precursors, e.g., II is described. This route makes it possible to synthesize analogs with various substituents at C-2 and C-5 of the hydroxyethylene isostere residue.

ACCESSION NUMBER: 1991:472189 CAPLUS
DOCUMENT NUMBER: 115:72189
TITLE: Synthesis of renin inhibitors possessing hydroxyethylene isostere residue from 3,4,6-tri-Q-acetyl-D-glucal via lactone precursor
AUTHOR(S): Shiozaki, Masao; Kobayashi, Yoshiyuki; Hata, Tadashi; Furukawa, Youji
CORPORATE SOURCE: New Lead Res. Lab., Sankyo Co., Ltd., Tokyo, 140, Japan
SOURCE: Tetrahedron (1991), 47(16-17), 2785-800
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English

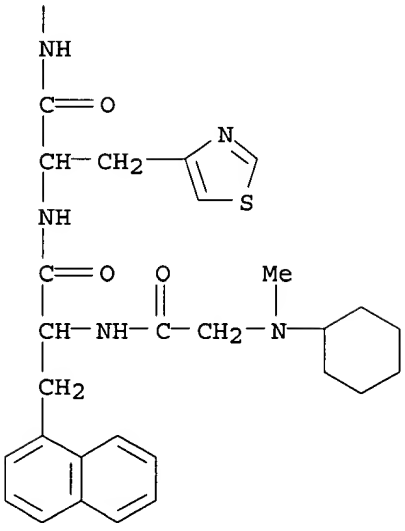
IT **135028-12-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and renin-inhibiting activity of)

RN 135028-12-5 CAPLUS
CN L-Alaninamide, N-cyclohexyl-N-methylglycyl-3-(1-naphthalenyl)-L-alanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-3-(4-thiazolyl)-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

PAGE 1-A



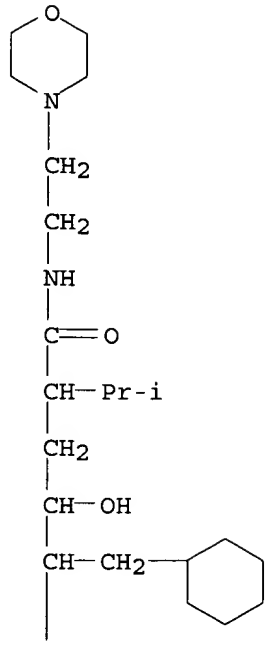
PAGE 2-A



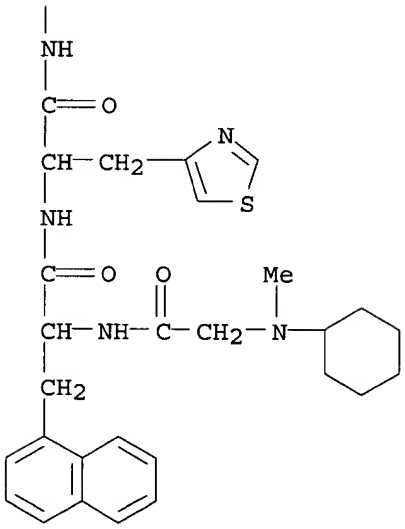
IT **134922-51-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., renin-inhibiting and antihypertensive activity of)
RN 134922-51-3 CAPLUS
CN L-Alaninamide, N-cyclohexyl-N-methylglycyl-3-(1-naphthalenyl)-L-alanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-3-(4-thiazolyl)-,

[1S-(1R*,2R*,4S*)]- (9CI) (CA INDEX NAME)

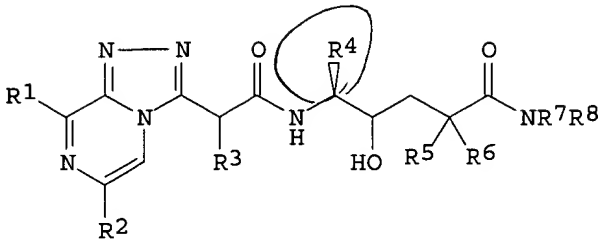
PAGE 1-A



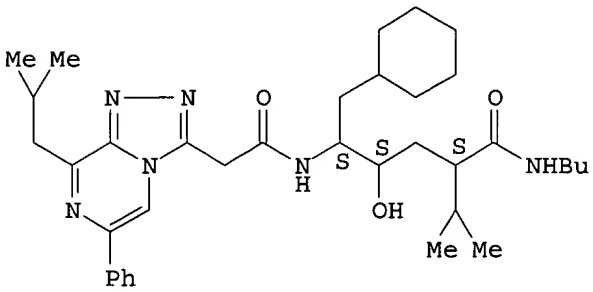
PAGE 2-A



L7 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I



II

AB The title compds. [I; R1 = alkyl, Ph; R2 = Ph, (alkyl)pyridyl; R3 = H, R9A; R4 = alkyl, cycloalkylalkyl; R5 = H, alkyl; R6 = H, alkyl(thio), alkoxy, OH, alkylsulfinyl, alkylsulfonyl, R10A1; R5R6 = alkylene; R7 = H, (hydroxy)alkyl; R8 = H, (hydroxy)alkyl, R11A2; R9 = pyridyl, imidazolyl, thiazolyl, pyrazolyl; R10 = alkoxy, alkenyl, Ph, OH; R11 = alkoxy, morpholino, thiomorpholino, piperidino, pyrrolidino, piperazinyl, (alkyl)pyridyl, (substituted) Ph, etc.; A = CH2, CH2CH2; A1, A2 = C1-4 alkylene], were prepd. as renin inhibitors. Thus, a mixt. of 8-isobutyl-6-phenyl-1,2,4-triazolo[4,3-a]pyrazin-3-ylacetic acid (prepn. from 2-aminoacetophenone and Na 4-methyl-2-oxopentanoate given), (2S,4S,5S)-5-amino-N-butyl-6-cyclohexyl-4-hydroxy-2-isopropylhexanamide (prepn. from isovaleric acid and (5R,4S)-3-benzyloxycarbonyl-4-cyclohexylmethyl-5-iodomethyl-2,2-dimethyl-1,3-oxazolidine given), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide.HCl, 1-hydroxybenzotriazole; and Et3N in DMF was stirred overnight to give amide II. I are useful in treating hypertension, congestive heart failure, and hyperaldosteronism. I (R1 = Pr, R2 = 3-pyridyl, other groups as in II) inhibited human plasma renin with IC50 = 2 .times. 10-10 M.

ACCESSION NUMBER: 1991:81884 CAPLUS
DOCUMENT NUMBER: 114:81884
TITLE: Preparation of (triazolopyrazinyl)acetamides as renin inhibitors
INVENTOR(S): Bradbury, Robert Hugh; Brown, David; Roberts, David Anthony; Waterson, David
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 369743	A2	19900523	EP 1989-311777	19891114
EP 369743	A3	19910911		
EP 369743	B1	19950419		
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
AU 8944354	A1	19900524	AU 1989-44354	19891102
AU 629867	B2	19921015		
ZA 8908361	A	19900829	ZA 1989-8361	19891102
CA 2002888	AA	19900517	CA 1989-2002888	19891114
US 5091425	A	19920225	US 1989-435687	19891114
JP 02204491	A2	19900814	JP 1989-297782	19891117
PRIORITY APPLN. INFO.:			GB 1988-26930	19881117
			GB 1989-12080	19890525

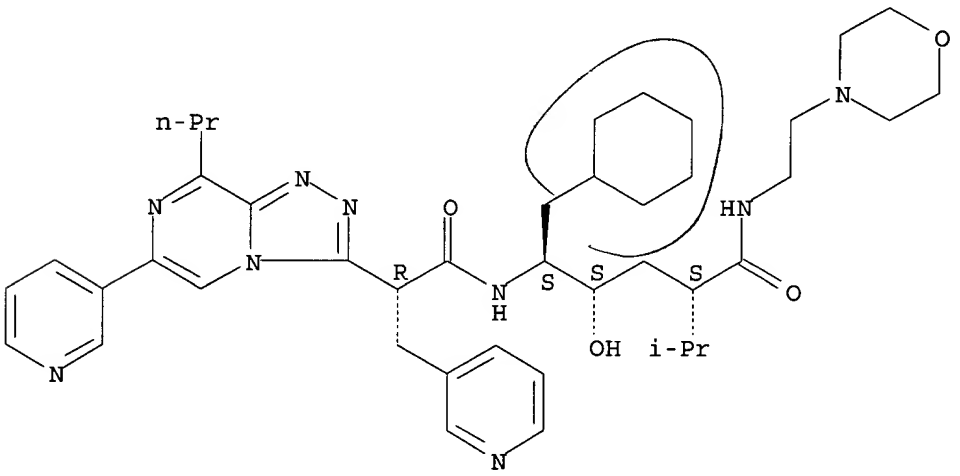
OTHER SOURCE(S): MARPAT 114:81884

IT **128901-39-3P 128948-65-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as renin inhibitor)

RN 128901-39-3 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine-3-acetamide, N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-8-propyl-6-(3-pyridinyl)-.alpha.-(3-pyridinylmethyl)-, [1S-[1R*(S*),2R*,4R*]]- (9CI) (CA INDEX NAME)

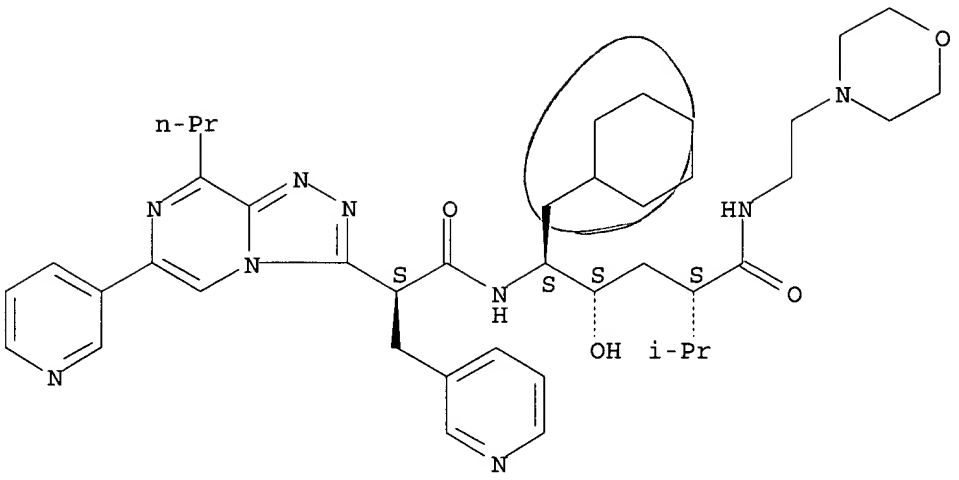
Absolute stereochemistry.



RN 128948-65-2 CAPLUS

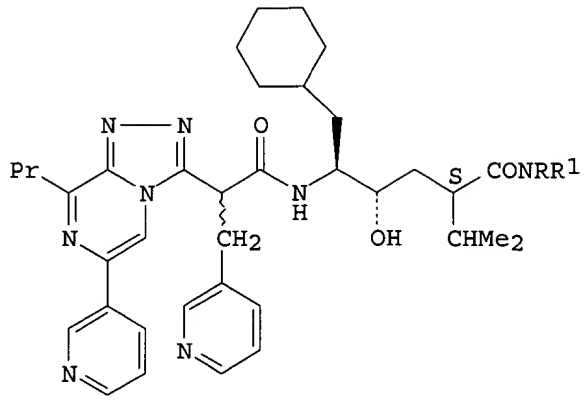
CN 1,2,4-Triazolo[4,3-a]pyrazine-3-acetamide, N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-8-propyl-6-(3-pyridinyl)-.alpha.-(3-pyridinylmethyl)-, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

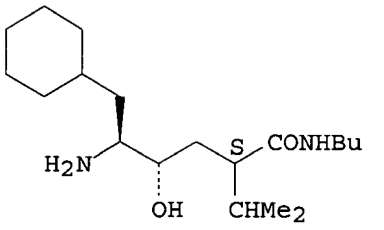

n-Pr
N
N
N
N
N
O
S
N
H
S
S
OH
S
i-Pr
HN
O
N
O
N
N

L7 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

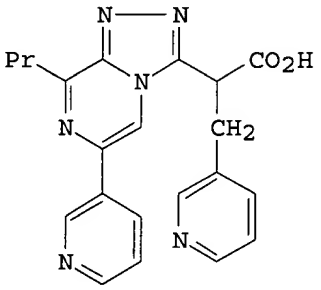
GI



I



II



III

AB Title peptide isosteres I [R = Bu, CH2CH2NMe2, CH2CH2NH2, morpholinoethyl, piperazinoethyl, 2-pyridylmethyl, (CH2)4OH, R1 = H; R = Bu, CH2CH2NMe2, R1 = Me; RR1 = (CH2CH2)2O] were prepd. as renin inhibitors. Thus, cyclohexane deriv. II was coupled with 1,2,4-triazolo[4,3-a]pyrazine deriv. III by EDCI to give I (R = Bu, R1 = H) (IV) as a mixt. of diastereoisomers. The more potent members of this series showed good inhibitory activity against partially purified human renin, IV for example, having an IC50 of 0.2 nM. Structure-activity relationships for these compds. were consistent with their binding to the S4-S2' sites of human renin.

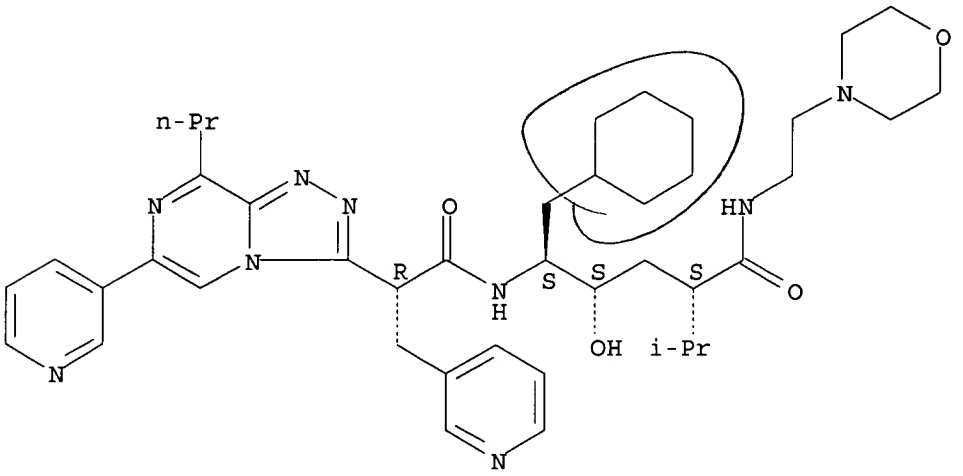
ACCESSION NUMBER: 1990:532798 CAPLUS
DOCUMENT NUMBER: 113:132798
TITLE: 1,2,4-Triazolo[4,3-a]pyrazine derivatives with human renin inhibitory activity. 2. Synthesis, biological properties and molecular modeling of hydroxyethylene isostere derivatives
AUTHOR(S): Bradbury, Robert H.; Major, John S.; Oldham, Alec A.; Rivett, Janet E.; Roberts, David A.; Slater, Anthony M.; Timms, David; Waterson, David
CORPORATE SOURCE: Dep. Chem., ICI Pharm., Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Journal of Medicinal Chemistry (1990), 33(9), 2335-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:132798
IT **128901-39-3P 128948-65-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and renin-inhibiting activity of)

RN 128901-39-3 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine-3-acetamide, N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-8-propyl-6-(3-pyridinyl)-.alpha.-(3-pyridinylmethyl)-, [1S-[1R*(S*),2R*,4R*]]- (9CI) (CA INDEX NAME)

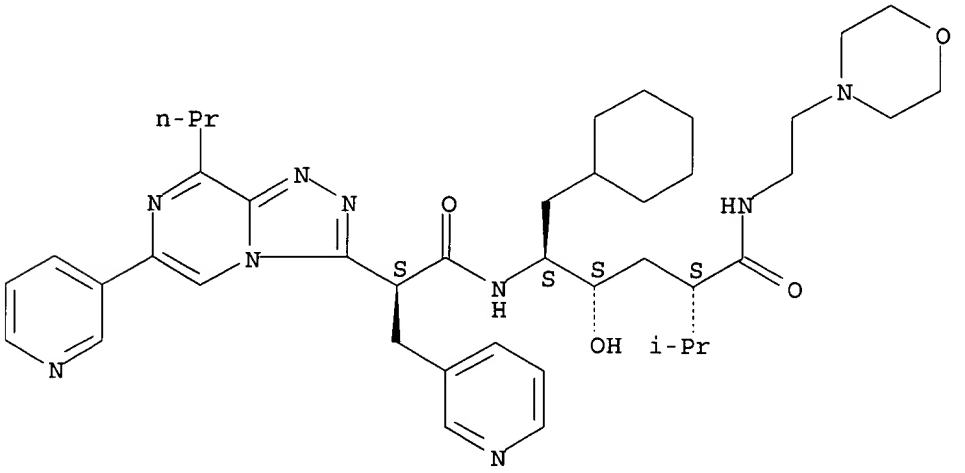
Absolute stereochemistry.



RN 128948-65-2 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine-3-acetamide, N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-8-propyl-6-(3-pyridinyl)-.alpha.-(3-pyridinylmethyl)-, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB HET-CONHCHR1CH(OH)CH2CHR2CONHR3 [I; HET = hydroquinolinyl, imidazopyridyl, hydroxyquinoxalinyl, dichloropyrrolyl, pyrrolopyridyl, (un)substituted indolyl; R1 = C6-8 cycloalkyl, Me2CH; R2 = C3-5 alkyl, Ph, MeCH:CH, Me2C:CH, halovinyl,hydroxy C1-3 alkyl, amino C1-4 alkyl; R3 = C1-6 alkyl, morpholinoethyl] and their pharmaceutically acceptable salts, useful as antihypertensives (no data) were prepd. (2R,4S,5S)-6-Cyclohexyl-5-amino-2-(2'-chloro-2'-propenyl)-.gamma.-hexanolactone hydrochloride (165.5 mg) was coupled with 97.8 mg 5-chloroindole-2-carboxylic acid in the presence of N-methylmorpholine, N-hydroxybenzotriazole and dicyclohexylcarbodiimide in CH2Cl2 to give 226 mg (2R,4S,5S)-I (HET = 5-chloroindol-2-yl; R1 = cyclohexyl; R2 = ClC:CH2; R3 = Me).

ACCESSION NUMBER: 1990:35678 CAPLUS
DOCUMENT NUMBER: 112:35678
TITLE: Preparation of heterocyclyl nonpeptidic renin inhibitors as antihypertensives
INVENTOR(S): Rosati, Robert Louis
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 321192	A2	19890621	EP 1988-311798	19881214
EP 321192	A3	19910130		
EP 321192	B1	19931027		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4923864	A	19900508	US 1988-261878	19881024
JP 01250345	A2	19891005	JP 1988-313642	19881212
JP 06092366	B4	19941116		
PL 152507	B1	19910131	PL 1988-276363	19881212
CS 274671	B2	19910915	CS 1988-8203	19881212
ZA 8809307	A	19900829	ZA 1988-9307	19881213
CA 1314545	A1	19930316	CA 1988-585722	19881213
HU 48277	A2	19890529	HU 1988-6423	19881214
HU 201564	B	19901128		
AU 8826881	A1	19890615	AU 1988-26881	19881214
AU 593181	B2	19900201		
FI 8805783	A	19890616	FI 1988-5783	19881214
FI 88295	B	19930115		
FI 88295	C	19930426		
NO 8805549	A	19890616	NO 1988-5549	19881214
NO 172935	B	19930621		
NO 172935	C	19930929		
CN 1034366	A	19890802	CN 1988-108575	19881214
CN 1025676	B	19940817		
DK 8806948	A	19890811	DK 1988-6948	19881214
DD 283381	A5	19901010	DD 1988-323142	19881214
SU 1651786	A3	19910523	SU 1988-4613032	19881214
AT 96433	E	19931115	AT 1988-311798	19881214
ES 2059540	T3	19941116	ES 1988-311798	19881214

PRIORITY APPLN. INFO.: US 1987-132373 19871215
EP 1988-311798 19881214

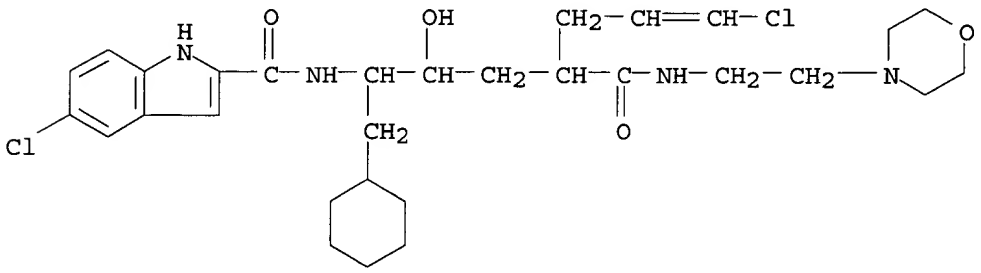
OTHER SOURCE(S): CASREACT 112:35678; MARPAT 112:35678

IT **124185-01-9P 124185-03-1P 124185-04-2P**
124206-43-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antihypertensive)

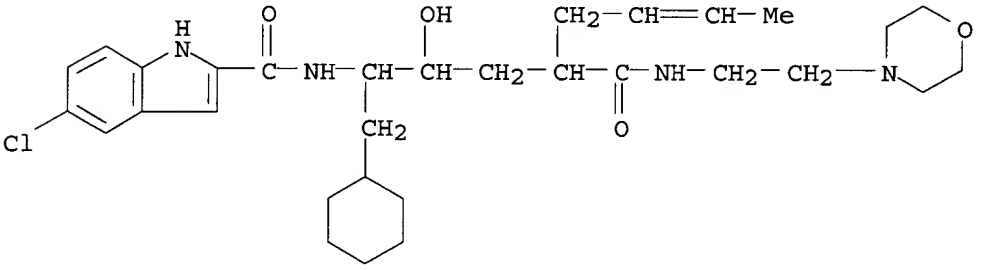
RN 124185-01-9 CAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[7-chloro-1-(cyclohexylmethyl)-2-hydroxy-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]-6-heptenyl]-, [1S-(1R*,2R*,4S*)]- (9CI) (CA INDEX NAME)



RN 124185-03-1 CAPLUS

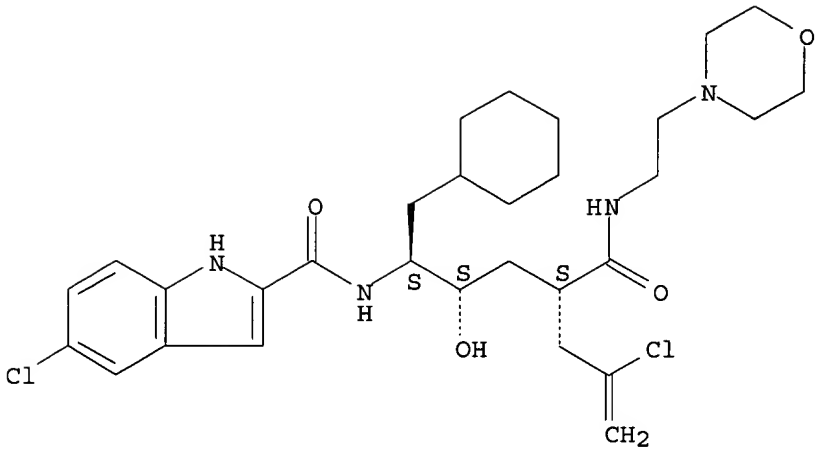
CN 1H-Indole-2-carboxamide, 5-chloro-N-[1-(cyclohexylmethyl)-2-hydroxy-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]-6-octenyl]-, [1S-(1R*,2R*,4S*)]- (9CI) (CA INDEX NAME)



RN 124185-04-2 CAPLUS

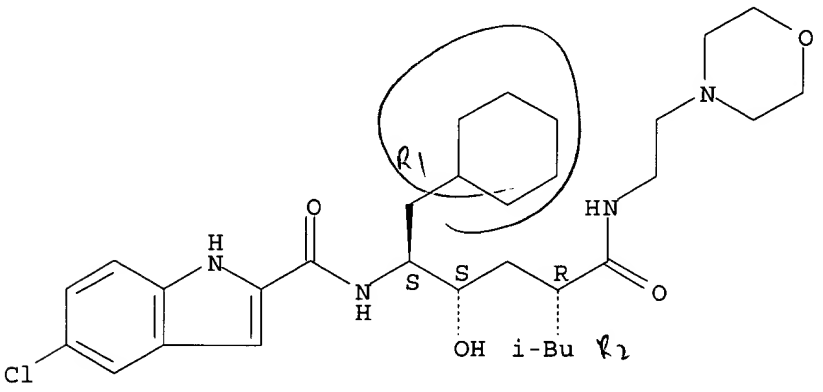
CN 1H-Indole-2-carboxamide, 5-chloro-N-[6-chloro-1-(cyclohexylmethyl)-2-hydroxy-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]-6-heptenyl]-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 124206-43-5 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[1-(cyclohexylmethyl)-2-hydroxy-6-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]heptyl]-, [1S-(1R*,2R*,4S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



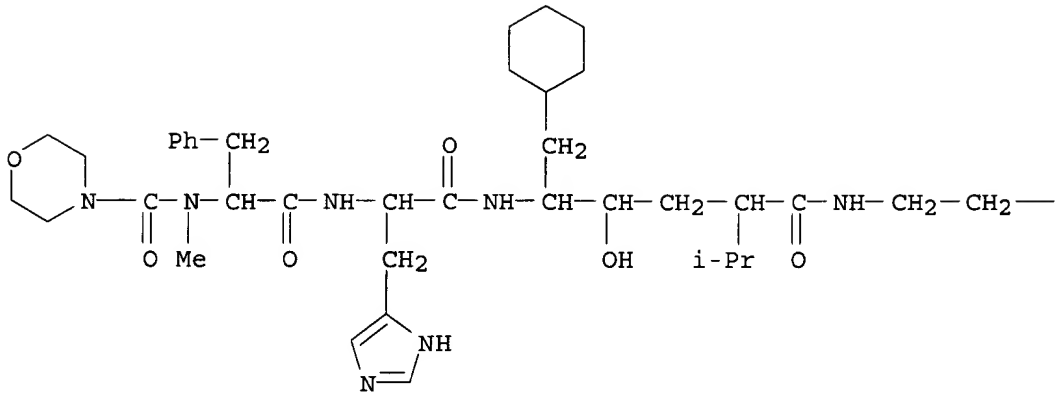
L7 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI For diagram(s), see printed CA Issue.
AB Tripeptides A-B-E-G-J [I; A = H, RCHR1NR2CO, RCHR1NR2SO2, substituted H2NCO or H2NSO2; R = H, aryl, heterocyclyl, C3-8 cycloalkyl, arylsulfonylcarbamoyl, (un)substituted C1-4 alkyl, etc.; R1, R2 = H, C1-4 alkyl; or R1R2 = (CH2)3; B = NRCH[(CH2)rR3]CO, NHCR4[(CH2)rR3]CO, Q; r = 1-4; R3 = H, C1-4 alkyl, aryl, indolyl; R4 = C1-4 alkyl; E = NRCH[(CH2)rR2]CO, NRCH[(CH2)pS(O)t(CH2)rR5]CO; R5 = H, aryl, heterocyclyl, (un)substituted C1-4 alkyl; t = 0-2; p = 1, 2; G = Q1; R6 = H, C1-8 alkyl, (2-8 alkenyl, mono- or disubstituted C2-8 alkyl, (un)substituted C3-7 cycloalkyl; R7 = H, C3-6 alkyl, aryl, (un)substituted (3-7 cycloalkyl; X = CH(OH) CH(OH)CH2, CH(NHR8)CH2, CH(NHR8); R8 = H, C1-4 alkyl, alkanoyl, alkoxycarbonyl, etc.; J = Y(CH2)nR9, etc.; n = 0-5; Y = (un)substituted NH, O], useful for treating various forms of renin-assocd. hypertension and congestive heart failure, were prepd. Deprotection of BOC-His(DNP)-ACHPA-(2S)-NHCH2CHMeCH2Me [BOC = Me3CO2C, DNP = 2,4-(O2N)2C6H3, ACHPA = (3S,4S)-4-amino-5-cyclohexyl-3-hydroxypentanoic acid residue] with a methanolic HCl soln. followed by coupling with Q-Phe-OH (Q = morpholino) in CH2Cl2 contg. (Me2CH)2NEt and benzotriazolyloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP) gave, after treatment with PhSH in MeOH, Q-Phe-His-ACHPA-(2S)-NHCH2CHMeCH2Me. This inhibited renin with an IC50 of 5 .mu.M.

ACCESSION NUMBER: 1989:633678 CAPLUS
DOCUMENT NUMBER: 111:233678
TITLE: Preparation and testing of tripeptide renin inhibitors with N-terminal ureido or sulfamido groups
INVENTOR(S): Greenlee, William J.; Parsons, William H.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

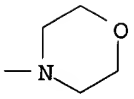
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 314239	A2	19890503	EP 1988-202334	19881019
EP 314239	A3	19901227		
R: CH, DE, FR, GB, IT, LI, NL				
JP 01149798	A2	19890612	JP 1988-272852	19881028

PRIORITY APPLN. INFO.: US 1987-113681 19871028
OTHER SOURCE(S): MARPAT 111:233678
IT **123600-21-5P 123600-24-8P 123600-47-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as renin-inhibitory antihypertensive)
RN 123600-21-5 CAPLUS
CN L-Histidinamide, N-methyl-N-(4-morpholinylcarbonyl)-L-phenylalanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

PAGE 1-A

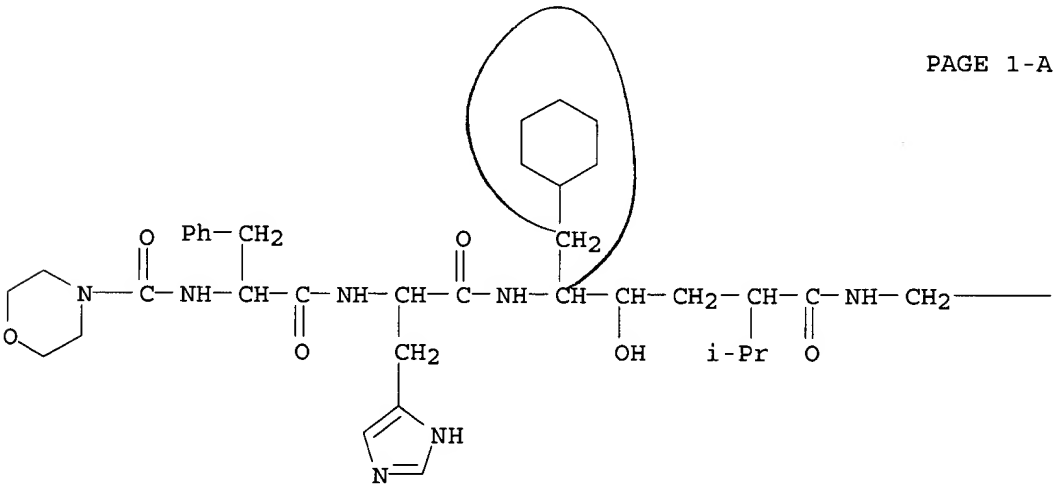


PAGE 1-B

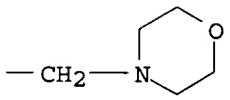


RN 123600-24-8 CAPLUS
CN L-Histidinamide, N-(4-morpholinylcarbonyl)-L-phenylalanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

PAGE 1-A

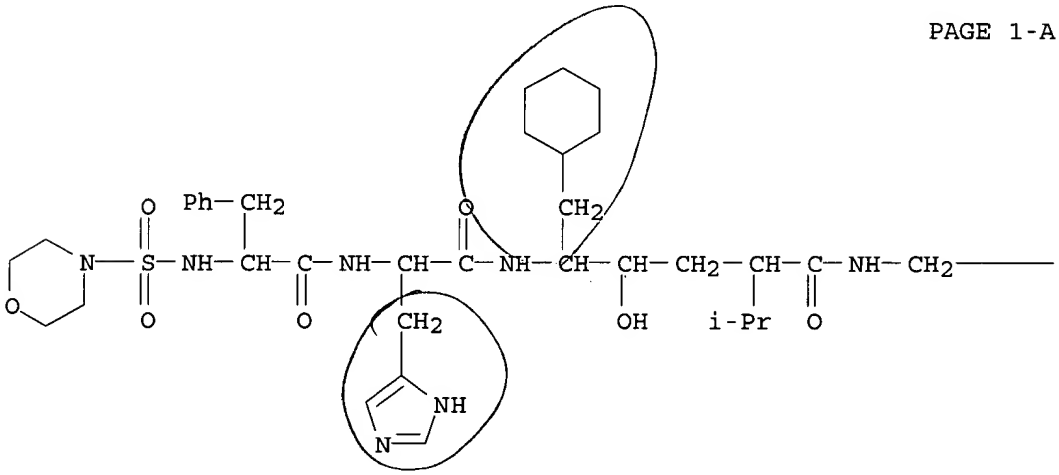


PAGE 1-B

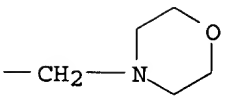


RN 123600-47-5 CAPLUS
CN L-Histidinamide, N-(4-morpholinylsulfonyl)-L-phenylalanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L7 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB R1S(O)m(CH2)nCHR2CONR3CHR4CONR5CHR6CH(OH)A [I; R1,R2,R4,R6 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, (bi)cyclic heterocyclic group contg. 1-4 heteroatoms chosen from N, S, and O; R3,R5 = H, alkyl; A = CH(OH)(CH2)qR7; R7 = R1, amino, alkylsulfonyl, etc.; m = 0-2; n = 1-5; q = 0-5], useful as renin inhibitors, were prepd. I are orally active antihypertensives with prolonged duration of action. L-N-[3-Ethylsulfonyl-2-(1-naphthylmethyl)propionyl]norleucine in DMF at -15.degree. was treated with Et3N, N3P(O)(OPh)2, and (2RS,3RS,4S)-4-amino-5-cyclohexyl-1-morpholino-2,3-pentanediol (prepn. given) in DMF. The mixt. was stirred overnight to give (2RS,3RS,4S)-4-[L-N-[3-ethylsulfonyl-2-(1-naphthylmethyl)propionyl]norleucyl]amino-5-cyclohexyl-1-morpholino-2,3-pentanediol (II). I inhibited human plasma renin in vitro with IC50's of 9.7 .times. 10-9-1.7 .times. 10-10 M. II at 30 ng/kg orally in marmosets reduced blood pressure by .apprx.20 mm Hg after .apprx.30 min. II at 10 mg/mg orally in rats showed plasma levels of 267 ng/mL after 30 min, 183 ng/mL after 1 h, and 34 ng/mL after 4 h.

ACCESSION NUMBER: 1989:633664 CAPLUS
DOCUMENT NUMBER: 111:233664
TITLE: Preparation and testing of N-acylamino acid amides as renin inhibitors
INVENTOR(S): Morishima, Hajime; Koike, Yutaka; Nakano, Masato; Atsuumi, Shugo; Tanaka, Seiichi; Matsuyama, Kenji
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 116 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 309766	A2	19890405	EP 1988-114374	19880902
EP 309766	A3	19900613		
EP 309766	B1	19980415		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 165085	E	19980515	AT 1988-114374	19880902
US 5122523	A	19920616	US 1988-240725	19880906
JP 02062856	A2	19900302	JP 1988-236728	19880921
JP 05087062	B4	19931215		
AU 8822992	A1	19890406	AU 1988-22992	19880929
AU 620820	B2	19920227		
CN 1032786	A	19890510	CN 1988-109019	19880929
US 5240924	A	19930831	US 1991-815412	19911231
US 5319082	A	19940607	US 1992-868140	19920414
US 5481036	A	19960102	US 1994-179195	19940110
US 5506356	A	19960409	US 1995-375738	19950120

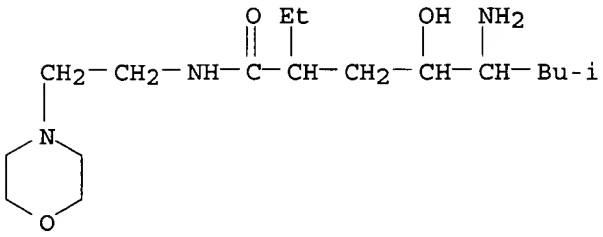
PRIORITY APPLN. INFO.:
JP 1987-244934 19870929
EP 1988-114374 19880902
US 1988-240725 19880906
US 1992-868140 19920414
US 1994-179195 19940110

OTHER SOURCE(S): MARPAT 111:233664

IT **123803-64-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation by, of [(naphthylmethyl)propionyl)]norleucine deriv., in prepn. of renin inhibitor)

RN 123803-64-5 CAPLUS
CN Octanamide, 5-amino-2-ethyl-4-hydroxy-7-methyl-N-[2-(4-morpholinyl)ethyl]-

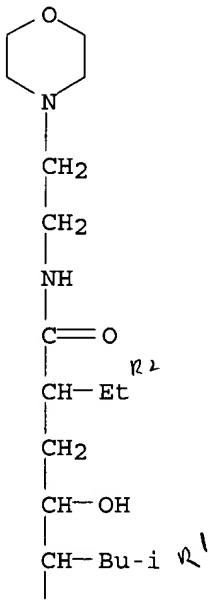
, dihydrochloride (9CI) (CA INDEX NAME)



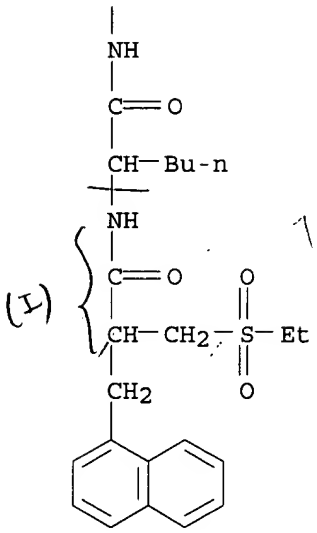
● 2 HCl

IT **123801-49-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as renin inhibitor)
RN 123801-49-0 CAPLUS
CN 1-Naphthalenepropanamide, .alpha.-[(ethylsulfonyl)methyl]-N-[1-[[[2-hydroxy-1-(2-methylpropyl)-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]amino]carbonyl]pentyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

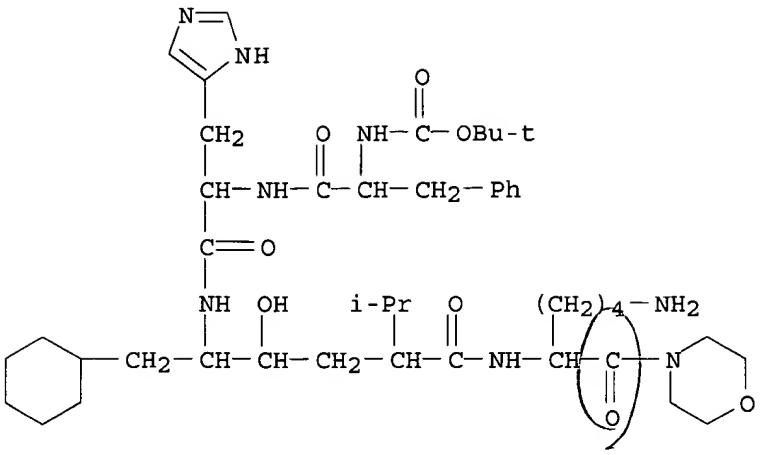


L7 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
GI For diagram(s), see printed CA Issue.
AB The title compds. [I; A = H, (substituted) carbamoyl, etc.; A1 = H, alkyl; r = 1-4; R1 = H, aryl, heterocyclylthiomethyl or -sulfinylmethyl, etc.; R3 = H, alkyl, aryl, indolyl; R4 = H, alkyl, alkenyl, etc.; R7 = alkyl, aryl, cycloalkyl, etc.; R9 = (substituted) aminoalkyl; R10 = H, alkyl; R11, R12 = H, alkyl; J = (substituted) alkylamino, etc.; Q = CH(OH), CH(NHR8), CH(OH)CH2, CH(NHR8)CH2; R8 = C1-4 alkyl, CHO, aroyl, etc.] and their pharmaceutically acceptable salts, useful as renin inhibitors, are prepd. BOC-Phe-His-ACHPA-Lys-NHCH2Q [Q = 4-pyridyl, ACHPHA = (3S,4S)-4-amino-5-cyclohexyl-3-hydroxypentanoic acid residue] was prepd. via condensation of H-ACHPA-OEt.HCl (prepn. given) with BOC-Phe-His(BOC)-OH in CH2Cl2 contg. 1-hydroxybenzotriazole and (Me2CH)2NEt, condensation of BOC-Phe-His-ACHPA-NHNH2 with H-Lys(Z)-NHCH2Q.CF3CO2H (prepn. given), and subsequently deprotection.

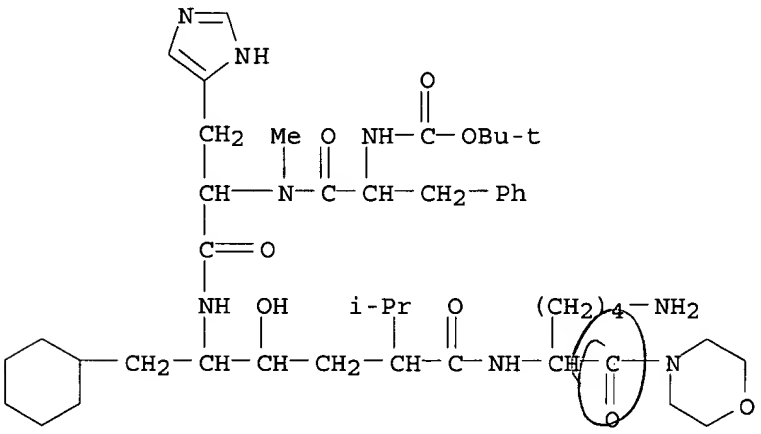
ACCESSION NUMBER: 1989:574670 CAPLUS
DOCUMENT NUMBER: 111:174670
TITLE: Tetrapeptides as renin inhibitors
INVENTOR(S): Chakravarty, Prasun K.; Greenlee, William J.; Parsons, William H.; Schoen, William
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 312157	A2	19890419	EP 1988-202210	19881005
EP 312157	A3	19900725		
R: CH, DE, FR, GB, IT, LI, NL				
JP 01143898	A2	19890606	JP 1988-256060	19881013

PRIORITY APPLN. INFO.: US 1987-107212 19871013
OTHER SOURCE(S): MARPAT 111:174670
IT **122959-00-6P 122959-06-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as renin inhibitor)
RN 122959-00-6 CAPLUS
CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[[5-amino-1-(4-morpholinylcarbonyl)pentyl]amino]carbonyl]-1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]-, [1S-[1R*,2R*,4R*(R*)]]- (9CI) (CA INDEX NAME)



RN 122959-06-2 CAPLUS
CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[[5-amino-1-(4-morpholinylcarbonyl)pentyl]amino]carbonyl]-1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]-N.alpha.-methyl-, [1S-[1R*,2R*,4R*(R*)]]- (9CI) (CA INDEX NAME)



L7 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN

AB R1-Z-NR2CHR3CHR4CH2CHR5COR6 I [R1 = H, acyl; R2 = H, alkyl; R3 = H, etherified hydroxyalkyl, acyloxyalkyl, cycloalkyl, etc.; R4 = OH, etherified or OH, acyloxy; R5 = alkyl, etherified hydroxyalkyl, acyloxyalkyl, cycloalkyl, etc.; R6 = substituted amino; Z = (N-alkyl) .alpha.-amino acid residue], useful as antihypertensives and cardiac stimulants (no data), were prepd. Thus, N-(2-quinolylcarbonyl)-L-phenylalanine was condensed with Me2CHCH2CH(NH2)CH(OH)CH2CH(CHMe2)CONHMe in the presence of hydroxybenzotriazole and N,N'-dicyclohexylcarbodiimide to give I [R1 = 2-quinolylcarbonyl, R2 = H, R3 = Me2CHCH2, R4 = OH, R5 = CHMe2, R6 = NHMe, Z = Phe]. Gelatin solns. were prepd. from N-[2-(R, S)-benzyl-5,5-dimethyl-4-oxohexanoyl]-His-Cha-cVal-NHBu [Cha = reduced L-cyclohexylalanyl, cVal = CH2CH(CHMe2)CO] 3 mg, gelatin 150.0 mg, phenol 4.7 mg, and water (to 1.0 mL total vol.).

ACCESSION NUMBER: 1987:19056 CAPLUS
DOCUMENT NUMBER: 106:19056
TITLE: 5-Amino-4-hydroxyvaleramide derivatives.
INVENTOR(S): Buehlmayer, Peter; Rasetti, Vittorio; Fuhrer, Walter; Stanton, James Lawrence; Goeschke, Richard
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 180 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 184550	A2	19860611	EP 1985-810523	19851108
EP 184550	A3	19880120		
EP 184550	B1	19920318		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4727060	A	19880223	US 1985-794914	19851104
AT 73778	E	19920415	AT 1985-810523	19851108
FI 8504434	A	19860514	FI 1985-4434	19851111
DD 239210	A5	19860917	DD 1985-282727	19851111
DK 8505202	A	19860514	DK 1985-5202	19851112
NO 8504516	A	19860514	NO 1985-4516	19851112
AU 8549821	A1	19860522	AU 1985-49821	19851112
AU 592768	B2	19900125		
JP 61122296	A2	19860610	JP 1985-252104	19851112
ZA 8508662	A	19860730	ZA 1985-8662	19851112
HU 39193	A2	19860828	HU 1985-4327	19851112
ES 548798	A1	19870501	ES 1985-548798	19851112
ES 557316	A1	19880401	ES 1987-557316	19870114
US 4931591	A	19900605	US 1989-380711	19890712
AU 8943855	A1	19900322	AU 1989-43855	19891027

PRIORITY APPLN. INFO.:

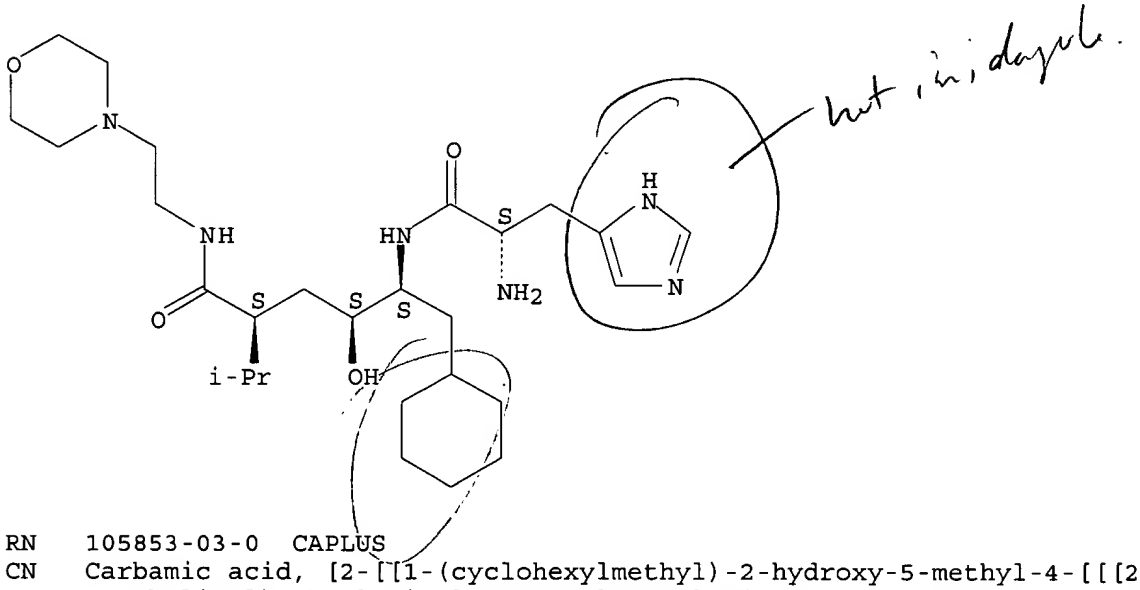
CH 1984-5426	19841113
CH 1985-3094	19850717
CH 1983-6285	19831123
US 1985-794914	19851104
EP 1985-810523	19851108
US 1987-123618	19871228

IT **105853-02-9P 105853-03-0P 105853-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of)

RN 105853-02-9 CAPLUS
CN 1H-Imidazole-4-propanamide, .alpha.-amino-N-[1-(cyclohexylmethyl)-2-

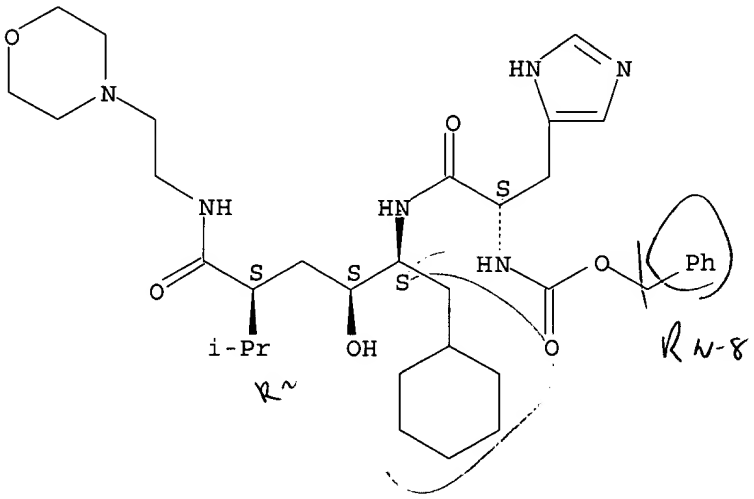
hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]-, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

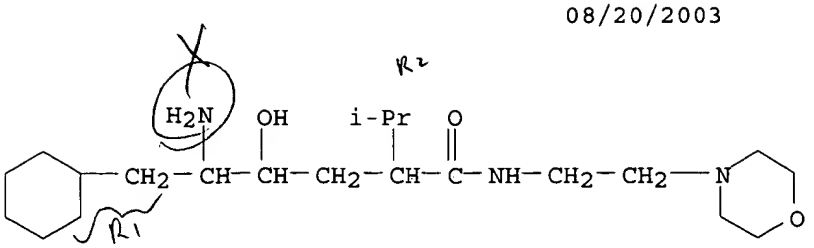


RN 105853-03-0 CAPLUS
CN Carbamic acid, [2-[[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-, phenylmethyl ester, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

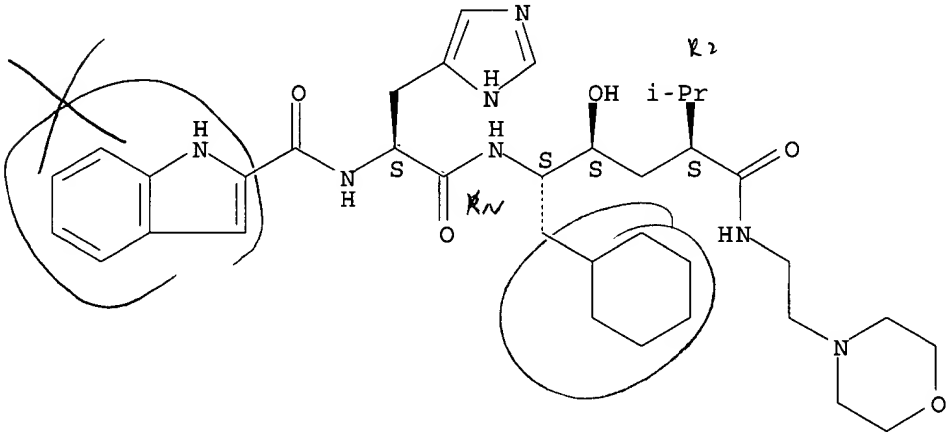


RN 105853-04-1 CAPLUS
CN Cyclohexanehexanamide, .delta.-amino-.gamma.-hydroxy-.alpha.-(1-methylethyl)-N-[2-(4-morpholinyl)ethyl]-, [.alpha.S-(.alpha.R*,.gamma.R*,.delta.R*)]- (9CI) (CA INDEX NAME)



IT **105852-14-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antihypertensive and cardiac stimulant)
RN 105852-14-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(cyclohexylmethyl)-2-hydroxy-5-methyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]hexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-, [1S-[1R*(R*),2R*,4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



```
=> d his

     (FILE 'HOME' ENTERED AT 16:10:23 ON 20 AUG 2003)

     FILE 'REGISTRY' ENTERED AT 16:10:37 ON 20 AUG 2003
L1              STRUCTURE UPLOADED
L2              STRUCTURE UPLOADED
L3           25 S L2
L4              STRUCTURE UPLOADED
L5            1 S L4
L6          107 S L4 FUL

     FILE 'CAPLUS' ENTERED AT 16:14:28 ON 20 AUG 2003
L7           22 S L6

=> log
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     100.63     250.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -14.32     -14.32

STN INTERNATIONAL LOGOFF AT 16:15:44 ON 20 AUG 2003
```